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# **THE ROLE OF SMOKING-RELATED BIOMARKERS IN SMOKING CESSATION**

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**Lion Shahab**

**A thesis submitted for the degree of *Philosophiæ Doctor***

**UNIVERSITY COLLEGE LONDON**

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## **DECLARATION**

I, Lion Shahab, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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## ABSTRACT

Much progress has been made in the field of tobacco control but the fact that the smoking prevalence in most Western countries is declining only slowly and still rising in many non-Western countries underlines the need to develop new ways to increase smoking cessation rates. Smoking-related biomarkers - biochemical, physiological or anatomical indices of exposure, risk and harm linked to smoke constituents - have been instrumental in furthering tobacco control, and this thesis examines the role of these biomarkers in smoking cessation. Study 1 evaluated whether biomarkers of exposure can be substituted by self-report and found that most smokers have only limited awareness regarding their level of exposure. Study 2 qualitatively explored smoking cessation in smokers and ex-smokers and examined their views on existing interventions in the NHS as well as on novel interventions involving biomarker feedback. Most participants commented positively on the Stop Smoking Services and welcomed the use of biomarkers in smoking cessation interventions. Study 3 tested the effectiveness of such an intervention adding feedback of an exposure and risk biomarker to brief advice in a randomised controlled trial. The intervention successfully altered cognitive antecedents of behaviour change but increased cessation rates only among smokers with high self-efficacy levels in comparison with the control group. Studies 4 and 5 used exposure and harm biomarkers from a nationally representative sample to determine smoking rates among people with objective signs of chronic obstructive pulmonary (COPD) or cardiovascular (CVD) diseases and to evaluate the potential impact of a diagnosis on smoking cessation. People with COPD but not CVD were more likely to smoke; a disease diagnosis was associated with higher motivation to stop among smokers with COPD and with higher cessation rates in smokers with a CVD. The importance of these findings for the measurement of smoke intake, improvement of interventions and detection and treatment of smokers with diseases is discussed.

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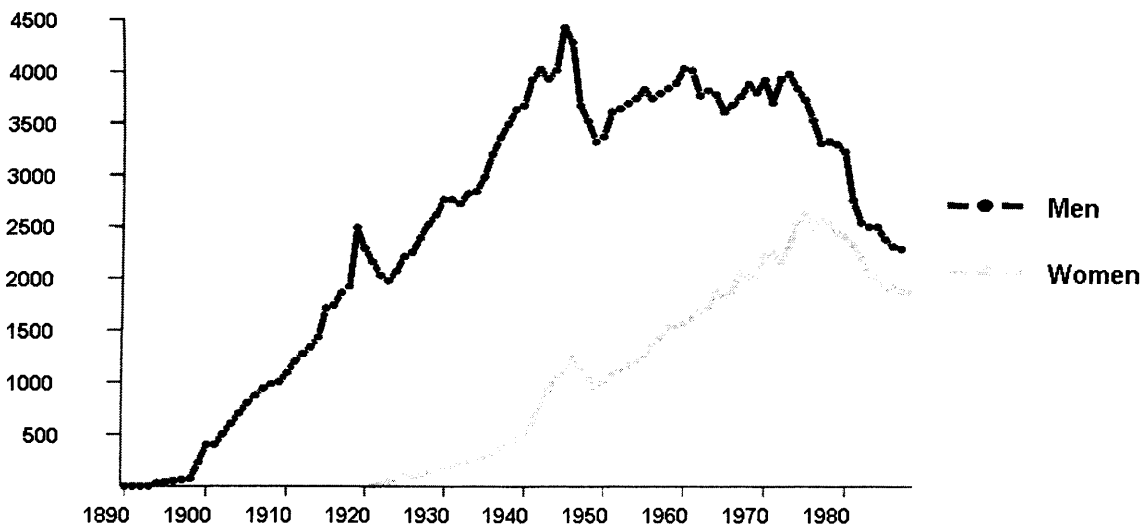
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## Chapter I

### General introduction

Tobacco originates in the Americas and has been used by American Indians for over 2000 years. With the discovery of America, tobacco became available in Europe, and in the 16<sup>th</sup> and 17<sup>th</sup> century was initially smoked in pipes, then as snuff and by the 19<sup>th</sup> century in the form of cigars (Royal College of Physicians, 2000). However, it was not until the invention of the manufactured cigarette, in the latter part of the 19<sup>th</sup> century, that smoking became a mass phenomenon. As can be seen in Figure I.I, shortly after the introduction of the manufactured cigarette in the UK by British American Tobacco at the turn of the last century, consumption in men greatly increased. Following the Suffragette movement, women who had traditionally been excluded from this market also started to smoke in great numbers, being specifically targeted by the tobacco industry.

**Figure I.I: Per capita cigarette consumption, UK 1890-1990**



Source: Nicolaides *et al*, 1993

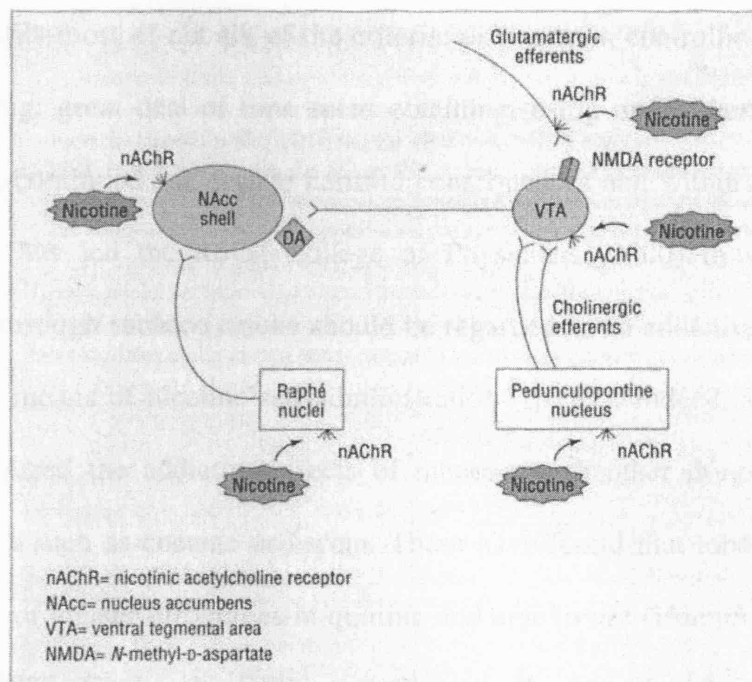
As cigarettes were also included in the ration packs of soldiers (indicated by the peaks in consumptions during the first and second world war in Figure I.I), smoking prevalence further increased so that in the late 40s an astonishing 65% of men and 40% of women were regular cigarette smokers (Royal College of Physicians, 2000);

however, it would be another ten years before the first reports of a link between smoking and lung cancer appeared.<sup>1</sup>

### 1.1 Smoking and addiction

The active substance in tobacco is nicotine, an alkaloid, which has pervasive effects on brain neurochemistry (Jarvis, 2004)<sup>2</sup>. Nicotine is rapidly absorbed through the alveoli in the lung into the pulmonary alveolar capillary and takes less than 20 seconds to reach the brain (Henningfield, Stapleton, Benowitz, Grayson *et al.*, 1993). Once it reaches the brain, nicotine preferentially binds to nicotinic acetylcholine receptors (nAChR), which are found throughout the body (Gotti, Fornasari, & Clementi, 1997). More specifically, nicotine binds to nAChR in the mesocorticolimbic dopaminergic system that projects from the ventral tegmental area to the nucleus accumbens and prefrontal cortex (Corrigall, Franklin, Coen, & Clarke, 1992).

**Figure I.II: Nicotine pathways of reinforcement and addiction<sup>#</sup>**



<sup>#</sup> Adapted from Watkins *et al.* (2000)

<sup>1</sup> One early study carried out in Nazi-Germany had been published in 1943 (Schairer & Schoniger, 2001) but was largely forgotten owing to the disruptions of war

<sup>2</sup> Yet, there are many more alkaloids present in tobacco smoke such as anatabine (Hoffmann, Djordjevic, & Hoffmann, 1997) and it is thought that other tobacco additives (e.g. ammonia) may reinforce the addictive effect of nicotine (Henningfield, Pankow, & Garrett, 2004)

Binding to the nAChR in the ventral tegmental area (and its presynaptic glutamatergic efferents) leads to *N*-methyl-D-aspartic-acid initiated burst firing in the mesolimbic pathway, which in turn results in an increased release of dopamine in the nucleus accumbens and the associated extended amygdala<sup>3</sup> (Watkins, Koob, & Markou, 2000). Although the exact mechanisms of dopaminergic action are debated (Berridge & Robinson, 1998), it is generally accepted that dopamine has a crucial role as a reward neurotransmitter (Wise & Rompre, 1989) and Figure I.II provides a schematic of the pathways mediating nicotine-induced positive reinforcement.

Animal models have shown the reinforcing effects of nicotine (e.g. Corrigall & Coen, 1989). Moreover, the addictive nature of nicotine is also corroborated by the psychological and behavioural consequences of smoking that can be observed in humans. Using DSM-IV or ICD-10 definitions of substance dependence, smoking clearly fulfils most, if not all, of the criteria: difficulty in controlling use; strong desire to take drug; great deal of time spent obtaining, using or recovering from effects of substance; continued use despite harmful consequences and withdrawal, to name but a few. This has led the Royal College of Physicians (2000) to state that “nicotine delivered through tobacco smoke should be regarded as an addictive drug, and tobacco use as the means of nicotine self-administration” (p. 87). Indeed, a number of studies have compared the addictive effects of nicotine with other drugs known to induce dependence such as cocaine or heroin. These have found that tobacco was associated with equal or greater difficulties in quitting and urge to use (Henningfield, Miyasato, & Jasinski, 1985; Kozlowski, Wilkinson, Skinner, Kent *et al.*, 1989) and that users of drugs may even misclassify intravenous nicotine as cocaine and, at high doses, as an

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<sup>3</sup> The extended amygdala consists of the central nucleus of the amygdala, the bed nucleus of the stria terminalis and the posterior part of the shell of the nucleus accumbens and has been implied in the modulation of drug reward (Koob, Sanna, & Bloom, 1998)



opiate (Jones, Garrett, & Griffiths, 1999). The highly addictive nature of tobacco was also acknowledged in the 1988 Report of the US Surgeon-General (1988), which concluded that “the pharmacological and behavioural processes that determine tobacco addiction are similar to those that determine drugs such as heroin and cocaine”. Thus, on the basis of current evidence, it is clear that tobacco dependence represents a very serious form of drug addiction and - considering the levels of worldwide cigarette consumption – one, which is arguably unlike any other in the scale of its societal impact.

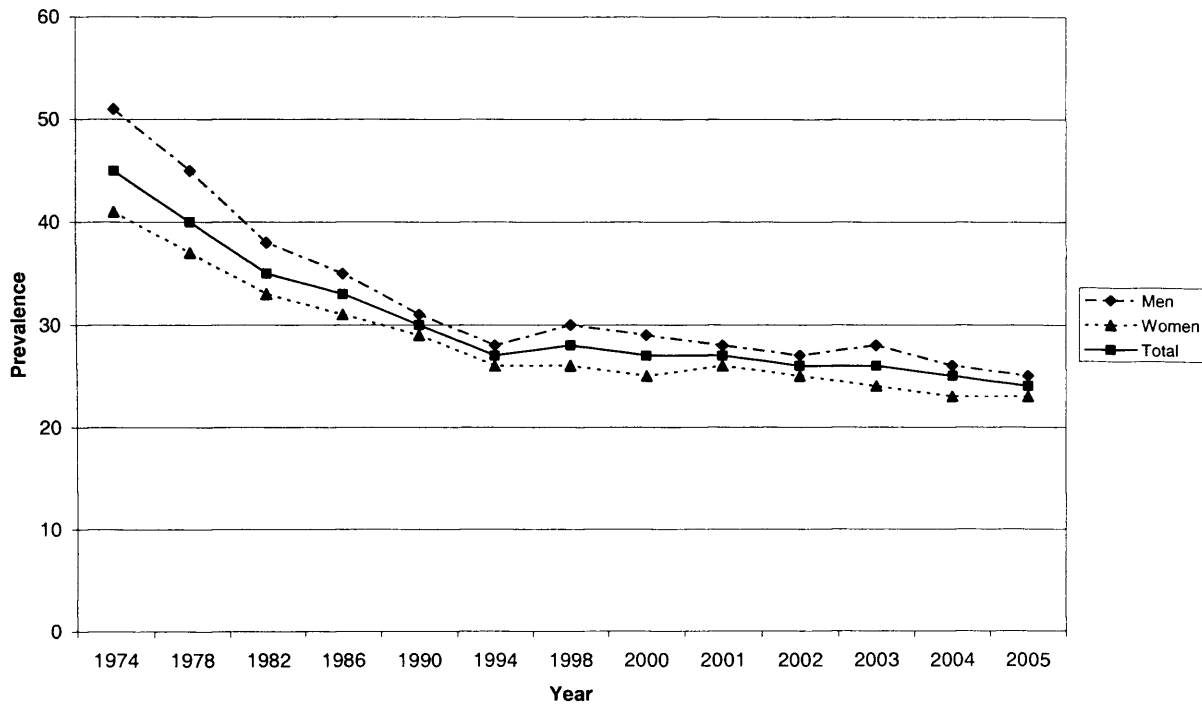
### ***1.ii Smoking prevalence<sup>4</sup>***

Tobacco use in the UK was initially recorded by the tobacco industry, and these data indicate that tobacco consumption reached a peak at 8.8 g per adult in 1945 and 1946; first smoking prevalence figures were released in 1948 showing that 65% of men and 40% of women were smokers (Nicolaidis, Wald, Forey, & Lee, 1993). Over the following decades, prevalence among men decreased slowly, but it continued to rise among women peaking in 1966 and 1969 at 44%.

With the introduction of the General Household Survey in 1972, industry-independent data become available. As can be seen in Figure I.III, prevalence figures steeply decreased since the 70s until the mid-90s when this decline started to level off. Smoking prevalence is currently falling by less than 0.4% per year (Jarvis, 2003) and the latest available survey data (2005) suggest an overall cigarette smoking prevalence in the UK of about 24 percent (Goddard, 2006).

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<sup>4</sup> Throughout this thesis, the term ‘smoking’ refers to cigarette smoking alone. When smoking is meant to refer to other forms of consumption (e.g. pipe or cigar), this will be made explicit.

**Figure I.III: UK smoking prevalence 1974-2005 by sex<sup>#</sup>**

<sup>#</sup>Data are weighted from 1998 onwards and come from the General Household Survey (Goddard, 2006)

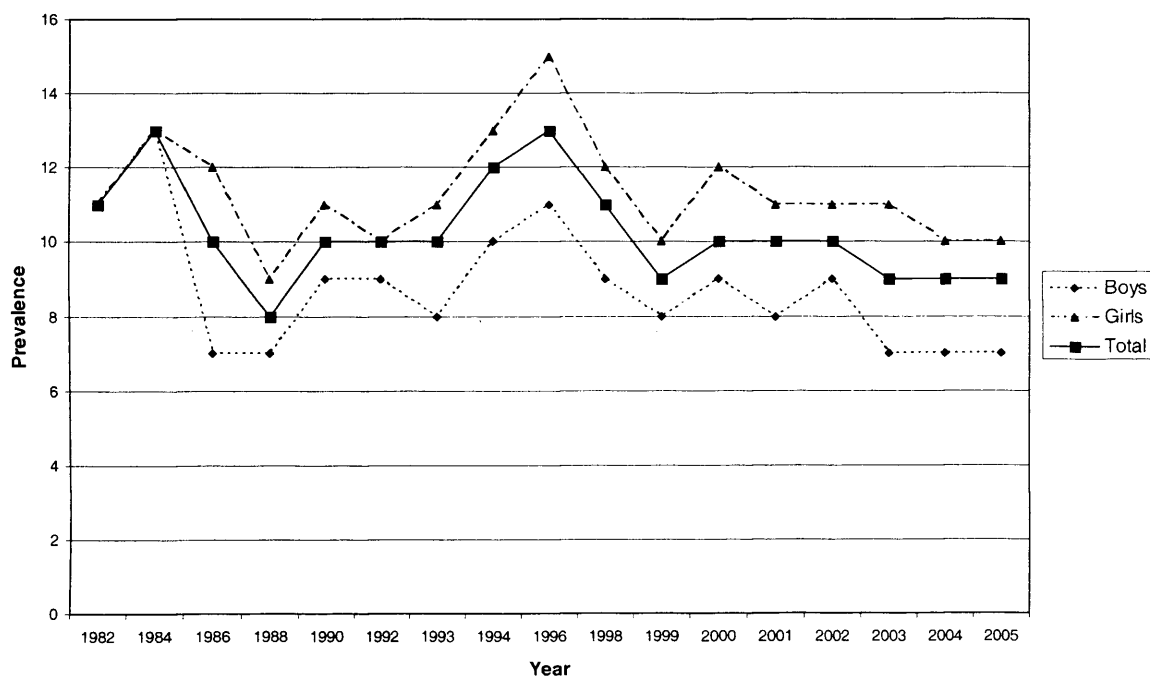
### **I.ii.i Smoking and gender**

As is evident from Figure I.III, across the last three decades consistently more men than women have been smoking. However, this gender gap in smoking prevalence has been much reduced over the years, such that by the mid-90s cigarette smoking prevalence of men and women converged to within one percentage point. On average men also tend to smoke slightly more cigarettes than women (14 vs. 13 in 2005), but on the basis of time to first cigarette women would appear to be more nicotine dependent than men (Lader & Meltzer, 2003). Of particular worry is smoking among pregnant women because of the teratogenic effects of smoke (Lichtensteiger, Ribary, Schlumpf, Odermatt *et al.*, 1988). Yet, smoking prevalence in this group appears to have remained stagnant, if not on the increase, over the last decade, and in 2005 nearly 33 percent of pregnant women were smokers of whom 17 percent smoked during pregnancy (Bolling, Grant, Hamlyn, & Thornton, 2007). The high smoking prevalence among pregnant women may in part be the result of the overall higher smoking prevalence among younger people (see next section).

### I.ii.ii Smoking and age

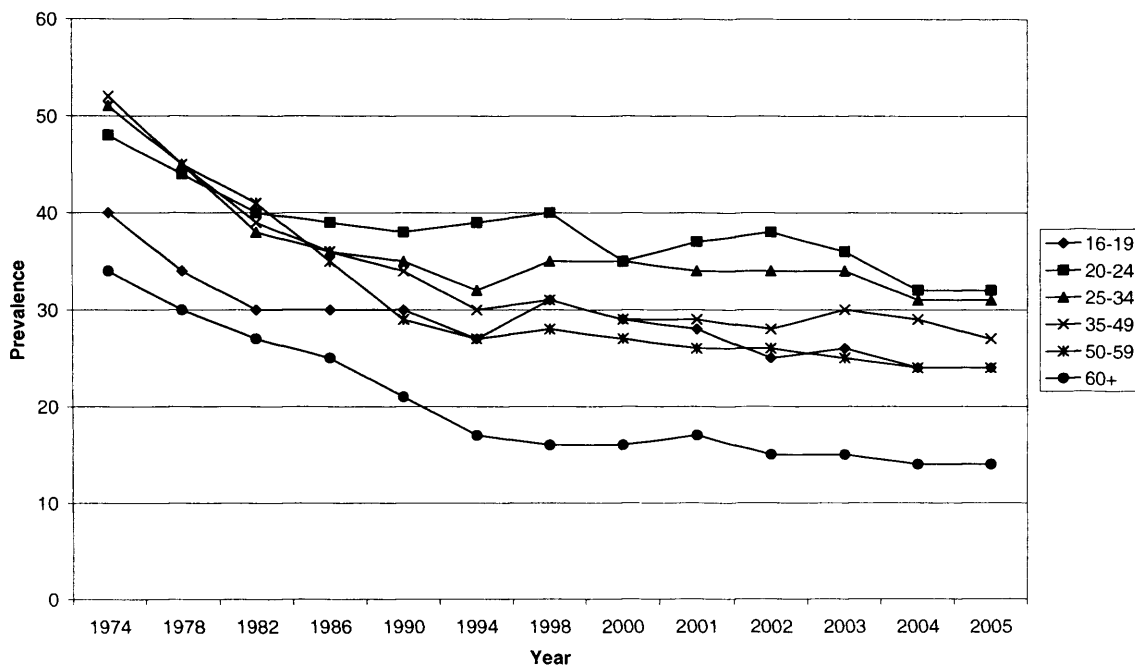
While men are overall more likely to be smokers than women, cigarette smoking prevalence is higher among girls than boys during adolescence (see Figure I.IV). Smoking is relatively rare among children below 11 years of age but becomes more commonplace in the years thereafter. Smoking prevalence among adolescents has remained relatively stable over the last couple of years after a slight increase during the 90s.

**Figure I.IV: UK smoking prevalence 1982-2005 in 11-15 year olds by sex<sup>#</sup>**



<sup>#</sup>Data come from the Smoking, Drinking and Drug Use Survey (Bates, Blenkinsop, Clemens, Deverill *et al.*, 2007)

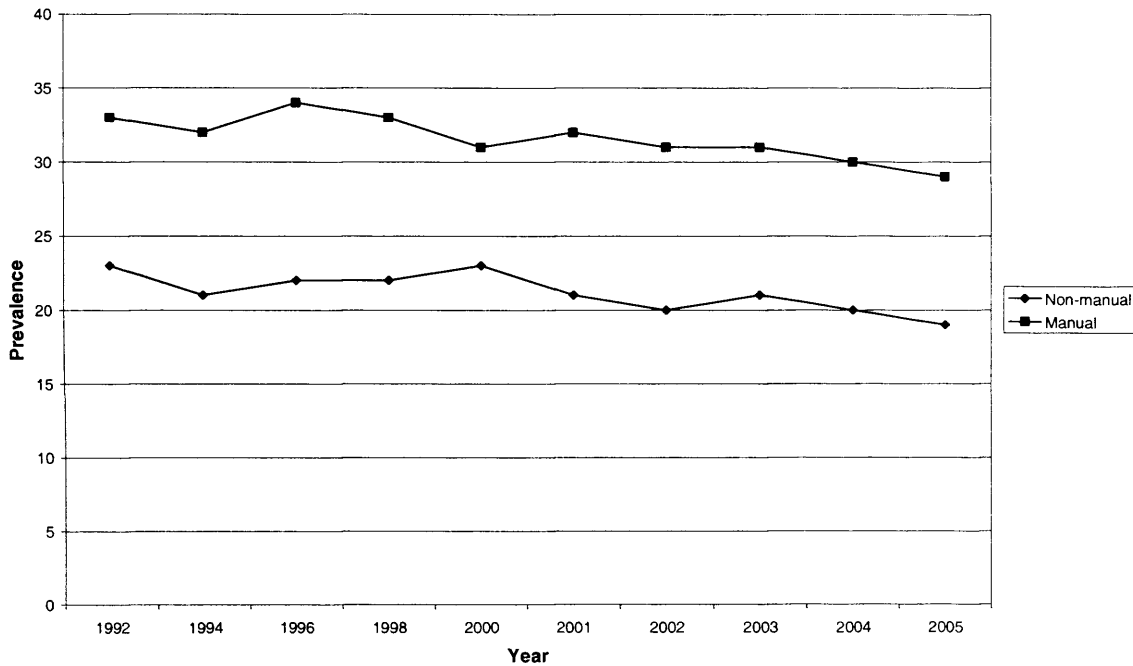
In general, smoking is most prevalent among younger age groups (20-24) progressively declining from then onwards. As can be seen in Figure I.V, although the smoking prevalence has decreased in all age groups since 1974, this effect has perhaps been most pronounced in older (50+) age groups.

**Figure I.V: UK smoking prevalence 1974-2005 by age<sup>#</sup>**

<sup>#</sup>Data are weighted from 1998 onwards and come from the General Household Survey (Goddard, 2006)

### **I.ii.iii Smoking and socio-economic status**

Smoking prevalence is strongly associated with socio-economic status (SES). Data suggest that only limited progress has been made in reducing the gap between the lowest and highest socio-economic groups and that while smoking prevalence was more than halved between 1973 and 2003 in the most advantaged groups, it has stayed virtually unchanged among those who are most deprived (Jarvis & Wardle, 2005). Similarly, smoking cessation rates are inversely related to deprivation; that is, the rate at which people in the highest socio-economic groups have stopped smoking has more than doubled over the last 30 years, while it has remained at the same level among those with the lowest socio-economic status. As Figure I.VI underlines, there still exists a ten percent difference in smoking prevalence between those in manual and non-manual occupations (a marker of SES).

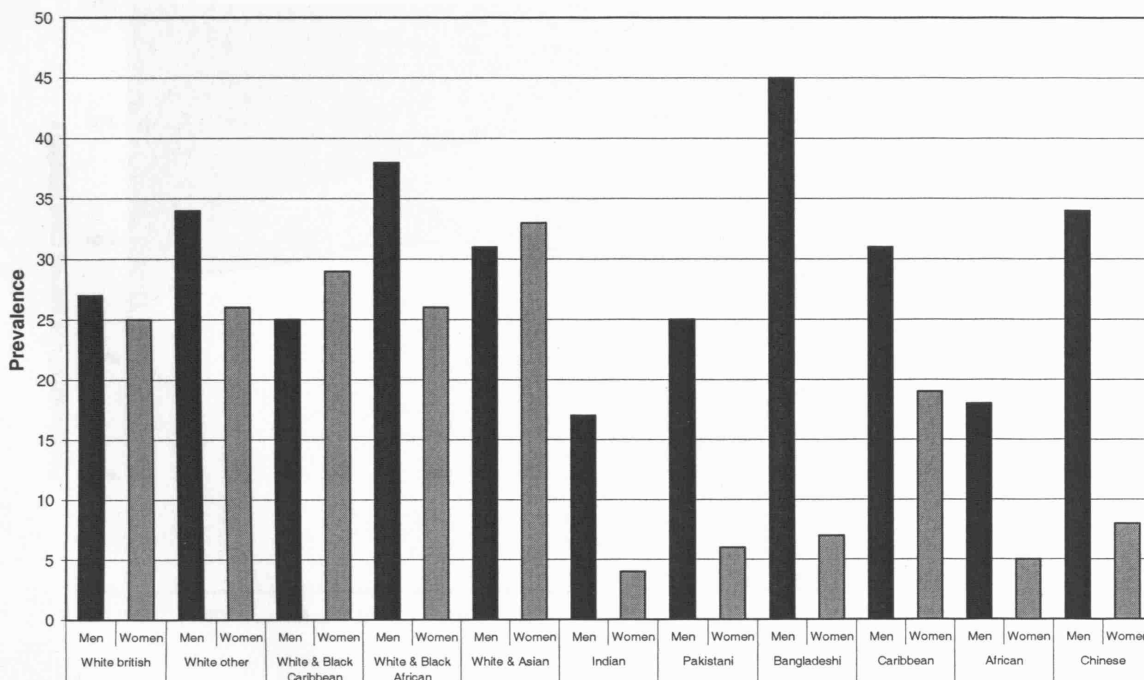
**Figure I.VI: UK smoking prevalence 1992-2005 by occupation<sup>#</sup>**

<sup>#</sup>Data are weighted from 1998 onwards and come from the General Household Survey (Goddard, 2006)

Although the SES differential has not changed much since 1992 - and is unlikely to disappear in the near future - some research has started to accumulate, which shows that owing to the greater use of the UK Stop Smoking Services by deprived smokers, this gap may be starting to close (Bauld, Judge, & Platt, 2007).

#### **I.ii.iv Smoking and ethnicity**

In general, cigarette smoking prevalence among minority ethnic groups is somewhat lower than among the UK population as a whole (Goddard, 2006). Yet, as shown in Figure I.VII, there exists a stronger gender bias for smoking in various ethnic minority groups. Thus, while the overall smoking prevalence for people originating from India or Pakistan may be low, this is not the case when looking at men and women separately. Indian and Pakistani women are much less likely to smoke than their male counterparts, who smoke at a rate only slightly below that of white British men. Similarly, Chinese, African, Caribbean or Bangladeshi men display a much higher smoking prevalence than women from these ethnic backgrounds.

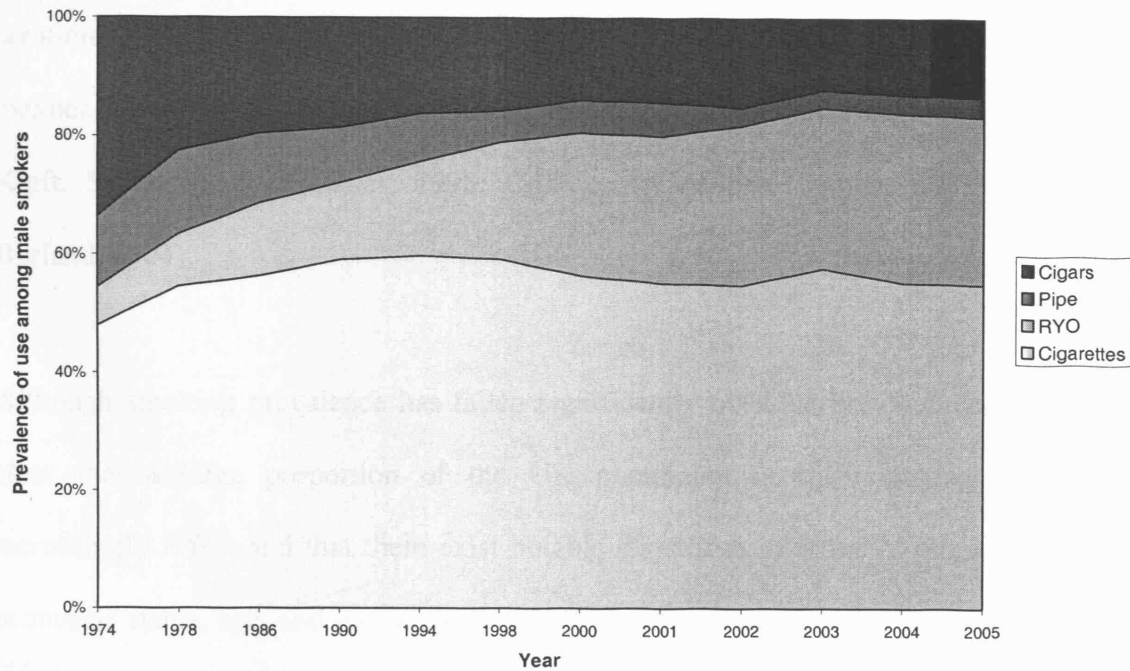
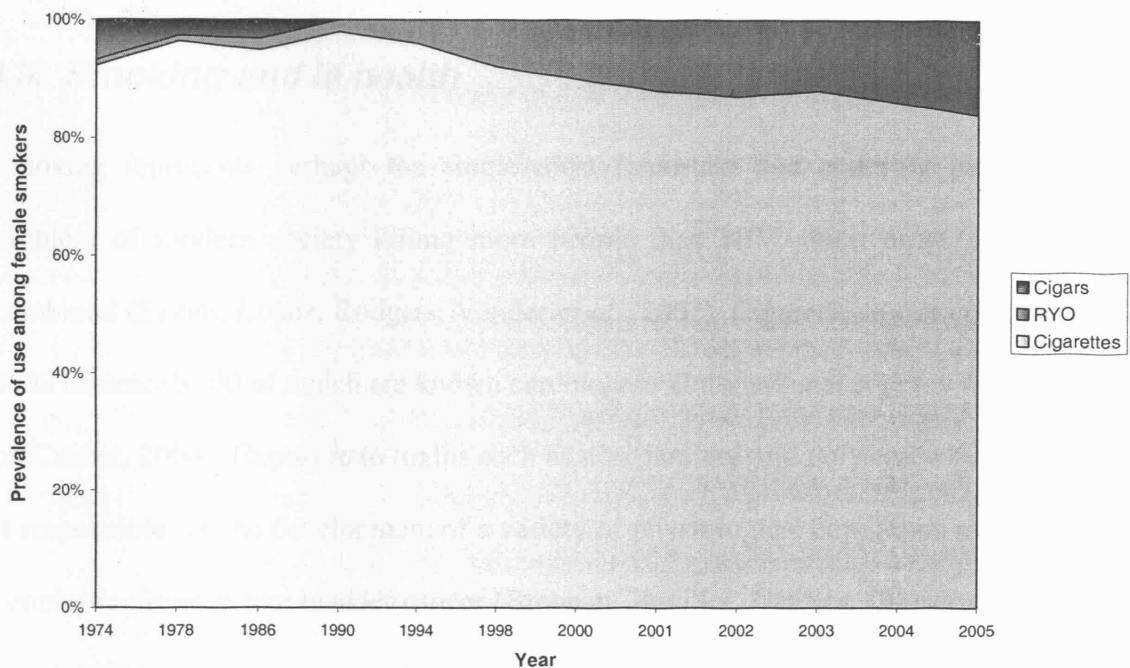
**Figure I.VII: UK smoking prevalence in 2005 by gender and ethnicity<sup>#</sup>**

<sup>#</sup>Data are weighted and come from the General Household Survey (Goddard, 2006)

Indeed, Bangladeshi men have the highest smoking prevalence among all UK ethnic groups at around 45%. People from a mixed race background, by contrast, display smoking rates at very similar levels to the overall UK population, with less difference between genders (Figure I.VII).

#### **I.ii.v Smoking and mode of delivery**

Thus far, this chapter has only concentrated on cigarette smoking. Obviously, however, there are other ways in which tobacco can be smoked – primarily in the form of cigars or pipes. The introduction of manufactured cigarette in the late 19<sup>th</sup> century was accompanied by a steep decline in the use of pipes and cigars, such that as early as 1919, cigarettes accounted for more sales by weight than all other tobacco products combined (Nicolaidis, Wald *et al.*, 1993). Figure I.VIII and Figure I.IX show that this downward trend in the use of cigars and pipes has continued to this date. Both account for less than 20% of male tobacco smokers, and there are virtually no female pipe or cigar smokers according to data from the General Household Survey.

**Figure I.VIII: Use of various tobacco products among men; 1974-2005<sup>#</sup>****Figure I.IX: Use of various tobacco products among women; 1974-2005<sup>#</sup>**

<sup>#</sup>Data are weighted from 1998 onwards and come from the General Household Survey (Goddard, 2006); RYO: roll-your-own; Categories are not mutually exclusive, i.e. smokers can report using more than one product

Both figures, however, also highlight an upward trend in the use of roll-your-own cigarettes (RYO; hand-rolled tobacco in sheet of thin paper with either a filter, no filter or a roach) over the last 30 years. This is most likely because manufactured cigarettes

are more highly taxed than RYO tobacco<sup>5</sup>. Thus, in tandem with recent increases in taxation, there has been a corresponding rise in the consumption of comparatively inexpensive RYO cigarettes, which has also been observed in other countries (e.g. Kraft, Svendsen, & Hauknes, 1998; Oddoux & Melihan-Cheinin, 2001; Scollo & Borland, 2004).

Although smoking prevalence has fallen significantly over the previous decades, it is clear that a large proportion of the UK population is still smoking cigarettes, increasingly RYO, and that there exist notable disparities in terms of ethnicity, socio-economic status, age, and less so, gender. All of these have important consequences for differential health outcomes among these different groups owing to the detrimental impact of smoking on health (Shahab, 2007), which will be discussed next.

### ***1.iii Smoking and ill health***

Smoking represents perhaps the single most important and enduring public health problem of modern society killing more people than HIV, illicit drugs and alcohol combined (Ezzati, Lopez, Rodgers, Vander *et al.*, 2002). Cigarette smoke contains over 4600 chemicals, 60 of which are known carcinogens (International Agency for Research on Cancer, 2004). Exposure to toxins such as nitrosamines and polycyclic hydrocarbons is responsible for the development of a variety of physiological conditions ranging from neoplastic diseases like bladder cancer (Brennan, Bogillot, Cordier, Greiser *et al.*, 2000) or oropharyngeal cancer (Elwood, Pearson, Skippen, & Jackson, 1984) to gastrointestinal problems like peptic ulcers (Smedley, Hickish, Taube, Yale *et al.*, 1988; Kato, Nomura, Stemmermann, & Chyou, 1992). Table I.I (adapted from West, 2006c)

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<sup>5</sup> In addition to a per unit duty, manufactured cigarettes are also taxed at 22 percent of the retail price (The Treasury, 2007)



provides an overview of fatal and serious non-fatal disorders for which tobacco use is a known or probable cause or exacerbating factor.

**Table I.I: Disorders and diseases linked to tobacco use**

<b>Smoking</b>		
Cancer of the lung	COPD <sup>1</sup>	Spontaneous abortion
Cancer of the larynx	Pneumonia	Stillbirth
Cancers of the oral cavity	Asthma attacks	Low birth weight
Cancer of the nasopharynx	Coronary heart disease	Conduct disorder <sup>2</sup>
Cancer of the oropharynx <sup>3</sup>	Aortic aneurism	SIDS <sup>4</sup>
Cancer of the oesophagus	Cerebrovascular disease	Low back pain
Cancer of the liver	Peripheral vascular disease	Osteoporosis
Cancer of the cervix	Vascular dementia	Tuberculosis
Cancer of the pancreas	Macular degeneration	Type II diabetes
Cancer of the stomach	Cataract	Peptic ulcer disease
Cancer of the urinary tract <sup>5</sup>	Hearing loss	Surgical complications
Leukemia	Infertility	
<b>Smokeless tobacco use<sup>6</sup></b>		
Cancer of the oral cavity	Cancer of the pancreas	

<sup>1</sup>chronic obstructive pulmonary disease, <sup>2</sup>in offspring of women who smoked during pregnancy, <sup>3</sup>and hypopharynx, <sup>4</sup>Sudden Infant Death Syndrome, <sup>5</sup>kidney, ureter and bladder, <sup>6</sup>these vary greatly in concentrations of carcinogens and therefore risk

Smoking causes approximately 30-40% of all deaths among the middle age population and reduces a smoker's life expectancy by an average of 10 years (Doll, Peto, Boreham, & Sutherland, 2004). In the USA, for instance, cigarette smoking is the leading preventable contributor to all-cause mortality (Centers for Disease Control and Prevention, 2002). The biggest killers for smokers are lung cancer, chronic obstructive pulmonary disease (COPD) and ischemic heart disease, which together account for approximately 63% of all smoking-related deaths in the UK (Office for National Statistics, 2002; National Ireland Statistics and Research Agency, 2002; General Register Office for Scotland, 2002). In 2000 alone, it is estimated that smoking was responsible for approximately 114.000 deaths in the UK (Peto, Lopez, Boreham, & Thun, 2006) and 5 million deaths worldwide (Ezzati & Lopez, 2003).

However, smoking not only contributes significantly to global mortality but also to morbidity. For each smoking-related death there are twenty smokers who suffer from

comorbid diseases; most commonly respiratory or cardiovascular diseases (CVD) or cancer (Hyland, Vena, Bauer, Li *et al.*, 2003). In addition, there is also a well-established link between smoking and psychological disorders (Upadhyaya, Deas, Brady, & Kruesi, 2002; West & Jarvis, 2005). For instance, smokers are much more likely than non-smokers to suffer from schizophrenia, depression and generalised anxiety disorder (Farrell, Howes, Bebbington, Brugha *et al.*, 2001). Explanations for this association tend to focus either on the causal role of mental disorders in the uptake of smoking, e.g. self-medication in schizophrenia (Dalack, Healy, & Meador-Woodruff, 1998), or on the possibility of an underlying common vulnerability to both mental disorders and smoking (Kendler, Neale, MacLean, Heath *et al.*, 1993). However, there is also some evidence from longitudinal and animal studies to suggest that smoking itself (or the psychotropics delivered by it) may have a causal role in the aetiology and onset of psychological disorders. Adolescents who smoke are at greater risk later in life to develop depression and anxiety (Choi, Patten, Gillin, Kaplan *et al.*, 1997; Isensee, Wittchen, Stein, Hofler *et al.*, 2003), and cigarette smoke has been found to decrease monoamine oxidase activity (Fowler, Volkow, Wang, Pappas *et al.*, 1996), which may increase a smokers susceptibility to subsequent schizophrenia and is consistent with the high smoking prevalence among schizophrenics (West & Jarvis, 2005).

Beside the physical and mental health impact that tobacco consumption has on the smoker, tobacco use also affects non-smokers who either directly inhale environmental tobacco smoke or, as foeti, ingest tobacco constituents in the womb. Research has shown a 15% excess health risk for non-smokers living with smokers (Hill, Blakely, Kawachi, & Woodward, 2004), and in the UK the number of deaths caused by passive smoking, which includes lung cancer, stroke and ischaemic heart disease, is estimated to have exceeded 10,000 in 2003 (Jamrozik, 2005). The effects of smoking on infants tend

to be more insidious – there is a link between smoking during pregnancy and low birthweight (Nieburg, Marks, McLaren, & Remington, 1985), cot death (Dwyer, Ponsonby, & Couper, 1999), but also cognitive impairment (Olds, Henderson, Jr., & Tatelbaum, 1994), attention deficit disorder (Fergusson, Horwood, & Lynskey, 1993) and delinquency in later life (Wakschlag, Pickett, Cook E Jr, Benowitz *et al.*, 2002).

### ***1.iv Health benefits of smoking cessation***

The health benefits of smoking cessation are considerable. Stopping smoking is arguably the single most important step a person can take to improve their well-being. Quitting smoking can prevent tobacco-related diseases within only a few years of cessation; it halves the risk of contracting lung cancer (Peto, Darby, Deo, Silcocks *et al.*, 2000) and has immediate positive effects on halting the occurrence and further development of various heart diseases (Rich-Edwards, Manson, Hennekens, & Buring, 1995). Smoking cessation has been shown to attenuate lung function decline (Anthonisen, Connett, Kiley, Altose *et al.*, 1994) and improve reproductive health (Lindley, Becker, Gray, & Herman, 2000; Peate, 2005). Ex-smokers are significantly less likely to suffer from post-operative complications than current smokers (Moller, Villebro, Pedersen, & Tonnesen, 2002), and there is evidence that quitting smoking may ameliorate mental health (Mino, Shigemi, Otsu, Tsuda *et al.*, 2000). The positive effects of smoking cessation are not only restricted to smokers themselves but also transfer to their surroundings through reduction of environmental tobacco smoke (Eisner, Smith, & Blanc, 1998; Wong, Hu, Lam, Hedley *et al.*, 1999; Hopkins, Briss, Ricard, Husten *et al.*, 2001).

The cost of smoking is very high indeed, both in terms of the direct and indirect health burden as discussed above but also in actual financial terms (Lightwood, Collins, Lapsley, & Novotny, 2000). Models predict that up to £12 million yearly could be saved

just in London hospitals if smokers could be convinced to stop smoking pre-operatively, and it is estimated that smoking costs the National Health Service at least £1.5 billion per year in England alone (Parrott & Godfrey, 2004); this excludes the immense costs arising from fires caused by smoking, the effects of passive smoking and smoking-related sick days.

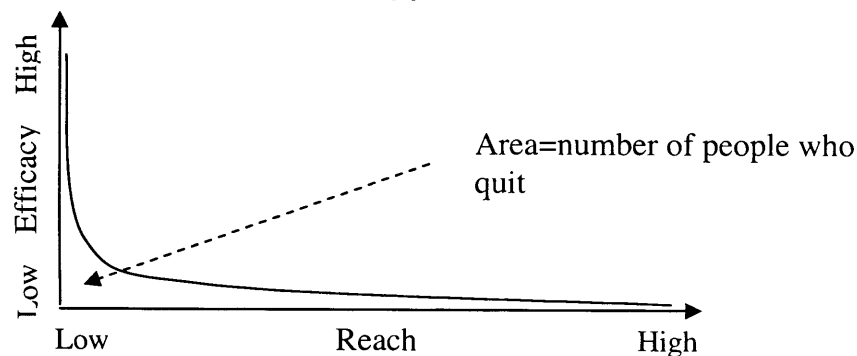
In light of the predictions of an ever increasing toll of smoking-related deaths over the coming decades throughout the world (Mackay, Eriksen, & Shafey, 2006), it is obvious that tobacco control plays a vital role in improving the health not only of the individual but of society as a whole.

### ***1.v Approaches to tobacco control***

Tobacco control takes many forms and its key elements can therefore be arranged in various different taxonomies. Tobacco control encompasses the various approaches to reduce the burden of tobacco on society. The aims of tobacco control are manifold (e.g. to reduce initiation of smoking, to increase cessation of smoking, to diminish toxicity of tobacco products) and the overarching outcomes or end goals that are assigned to tobacco control by people active in the field may differ substantially – from reducing smoking-related morbidity and mortality to eradicating addiction. It is not surprising then that there should be no single correct way of classifying tobacco control strategies. However, one intrinsically appealing distinction is one informed by the domain of action for tobacco control, i.e. strategies based on legislation and policy; on basic research, public awareness and values or on intervention programmes (Slama, 2004) with each of these strategies ranging along a continuum from an individual- to a population-based focus (e.g. Gruman & Lynn, 1993).

As a rule of thumb, there is an inverse relationship between the focus and efficacy of a specific approach (see Figure I.X). While an individual and more intensive approach (e.g. counselling) will lead to a higher cessation rate than a population and more cursory approach (e.g. raising taxes), it will also reach fewer people and therefore have a lower impact on overall smoking prevalence (Raw & McNeill, 1994).

**Figure I.X: Impact of tobacco control approach~**



~Based on Raw & McNeill (1994)

Common sense and current evidence suggest that the most successful strategies involve multiple approaches implemented in tandem within a comprehensive tobacco control scheme (World Health Organization, 1998; U.S.Department of Health and Human Services, 2000).

### **I.v.i Legislation and policy**

Legislation and policy approaches are likely to be very important for reducing global smoking prevalence in the future due to their wide-ranging impact (Levy, Chaloupka, & Gitchell, 2004). Among these, taxation arguably stands out as most effective (Aquilino & Lowe, 2004). Taxation tends to display price elasticity of between -0.3 and -0.5; that is, for a 10 % increase in taxes, there is an equivalent 3 to 5 % drop in cigarette demand (Levy, Cummings, & Hyland, 2000; Ranson, Jha, Chaloupka, & Nguyen, 2002). However, price elasticity is moderated by the characteristics of the smoker; young, pregnant smokers or low-income smokers are more likely to be responsive to taxation (Farrelly & Bray, 1998; Jha & Chaloupka, 1999; Ringel & Evans, 2001), and the effect

of taxation in low-and middle income countries is usually stronger than in high-income countries (The World Bank, 1999).

Another useful policy approach is the introduction of clean air laws, which have proven relatively effective when public and workplace smoking bans are comprehensive and are rigorously reinforced such as in the United States and Australia (Chapman, 1998; Levy & Friend, 2001). Although results from some studies indicate that stricter clean air laws can have an impact on smoking prevalence similar to price or tax increases (Stephens, Pederson, Koval, & Kim, 1997; Heloma, Jaakkola, Kahkonen, & Reijula, 2001), there is currently only limited evidence to support this notion.

Both banning of tobacco advertisements (Jha & Chaloupka, 1999) and reducing access to tobacco products have proven somewhat less useful for lowering smoking prevalence (Stead & Lancaster, 2000), and both need to be broad in scope in order to have an effect (Saffer & Chaloupka, 2000). Moreover, as these approaches are most likely to affect smoking initiation rather than cessation, it has to be kept in mind that they would be expected to have a delayed as opposed to immediate impact on smoking prevalence. In contrast, the way that cigarette packs themselves are presented may have an immediate negative influence on smoking initiation and instigate cessation (Borland, 1997; Wakefield, Morley, Horan, & Cummings, 2002). In Canada, for instance, results from one study support the effectiveness of larger and more graphic warning labels as smokers are more likely to quit following the introduction of new legislation to implement such warning labels (Hammond, Fong, McDonald, Cameron *et al.*, 2003), but again research is relatively limited.

The tobacco control community has to recognise that the increasing globalisation of tobacco companies requires national as well as international legislation, and tobacco subsidy and trade policies are a case in point. Especially relevant to European tobacco control is the quixotic substitution of tobacco farmers at a cost several hundred times that of monies made available by the European Union for smoking prevention (Joossens & Raw, 1996). While some progress appears to have been made in this area (Gilmore & McKee, 2002), a perhaps even more fruitful policy issue is the lobbying for trade restrictions (Raw & McNeill, 1994). Liberalisation of the tobacco trade has significantly raised cigarette consumption (The World Bank, 1999), especially so in new markets (Chaloupka & Laixuthai, 1996), and new legislation is needed to hinder and reverse unethical trade practices (Shaffer, Brenner, & Houston, 2005).

A last strand within legislation and policy approaches to tobacco control is the application of product regulation. Tobacco control policies that regulate products can be instrumental in preventing the engineering of more addictive tobacco products (West, 2006c). Considering the rising consumption of RYO cigarettes, one example of opportunity for product regulation is the current stance towards rolling tobacco, which comes under much less regulatory oversight than manufactured cigarettes despite evidence of equivalent or even more harmful effects compared with manufactured cigarettes (Bialous & Yach, 2001). Another possible way forward and a potentially opportune approach for product regulation is harm reduction. While this is not an uncontroversial issue, there is good evidence to suggest that the use of smokeless tobacco products like Swedish snus may reduce smoking-related mortality and increase cessation (Foulds, Ramstrom, Burke, & Fagerstrom, 2003; Ramstrom & Foulds, 2006). Likewise, the prolonged use of nicotine replacement therapy may provide a viable safe alternative to smoking (McNeill, Foulds, & Bates, 2001).

In the case of combustible products, it has been argued that cigarettes could be made safer by more tightly regulating tobacco constituents and imposing maximum yields of “toxin-to-nicotine” ratios of known carcinogens such as polycyclic aromatic hydrocarbons or tobacco-specific *N*-nitrosamines (Gray & Henningfield, 2004; WHO Study Group on Tobacco Product Regulation, 2004). However, due to the “light” cigarette disaster<sup>6</sup>, which is likely to have impeded tobacco prevention and increased smoking-related morbidity (Stratton, Shetty, Wallace, & Bondurant, 2001), the exact regulation of cigarette toxins remains a largely unresolved issue in current tobacco control.

### **I.v.ii Basic research, public awareness and values**

Social norms and coercion can have a powerful impact on behaviour, as for instance shown by changes (as well as the lack of changes) in sexually risky behaviour pattern following the AIDS epidemic (Hankins, 1998). In tobacco control, one of the most powerful social norms is the traditional taboo that exists in many countries against women’s smoking, which results in a much lower female smoking prevalence overall (West, 2006c). The eroding of these social norms, primarily due to aggressive marketing of the tobacco industry, therefore represents a real danger for future public health (Mackay & Amos, 2003).

Beyond traditional values that have influenced smoking prevalence, there has, of course, also been a tangible shift in both public perception and smoking prevalence as a consequence of smoking bans, health education, research and general mass media campaigns (Jha & Chaloupka, 1999). Making the public aware of the health

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<sup>6</sup> The tobacco industry was able to maximise the potential of ‘light’ cigarettes by marketing them as a healthier alternative thus leading many people to switch from regular to low tar cigarettes instead of quitting altogether



consequences of smoking through the publication of evidence for the link between smoking and lung cancer by researchers in the UK (Doll & Hill, 1950) and US (Wynder & Graham, 1950) and through thousands of subsequent studies (Surgeon General, 1989) has undoubtedly changed public health awareness in most, if not all, countries in the world (Warner, 2005). Research investigating the health effects of passive smoking was instrumental for the introduction of smoke-free laws in many states in the US (National Cancer Institute, 1999) and has also led to decreased smoking in private homes (Soliman, Pollack, & Warner, 2004).

Moreover, the accumulation of research evidence on the health effects of smoking has been crucial for the persuasion of health professionals to get behind the aims of tobacco control. There is no question that health professionals are extremely influential in reaching smokers and communicating the health message (Lancaster & Stead, 2004), and thanks to the early published studies on lung cancer, smoking was quickly considered as a serious health problem by health professional organisation such as the American Medical Association (Lundberg, 1985) and the Royal College of Physicians (Raw, White, & McNeill, 1990).

In terms of norms and values, as smoking prevalence is reduced, it becomes socially less acceptable and public tolerance of smoking decreases (Poland, Cohen, Ashley, Adlaf *et al.*, 2000; Wisotzky, Albuquerque, Pechacek, & Park, 2004), which in turn favours a positive climate for tobacco control activities and thus reduces smoking rates even further (Woodruff, Rosbrook, Pierce, & Glantz, 1993; Alamar & Glantz, 2006). However, research alone does not precipitate knowledge to the whole community due to a variety of socio-demographic factors. One important predictor of tobacco use cessation is education and the ability to access information (Wetter, Cofta-Gunn, Irvin,

Fouladi *et al.*, 2005). Not only may deprived smokers - given their stretched resources - feel that they have more urgent and pressing needs than smoking cessation, but they may also be less aware of smoking-related health risks (Hansen & Malotte, 1986) and the effectiveness of existing cessation treatment than affluent smokers (Roddy, Antoniak, Britton, Molyneux *et al.*, 2006). For this reason more aggressive targeted media marketing campaigns may be required. Long-term, intensive media counter-advertising campaigns seem to have the greatest overall impact on smoking prevalence (Centers for Disease Control and Prevention, 2000). Altogether, mass media campaigns can have good efficacy - reducing per capita consumption by about 13% and smoking prevalence by about 2.2 %, but this includes substantial variations depending on the particular type of campaign employed (Hopkins, Briss *et al.*, 2001).

Litigation and whistle-blowing within the tobacco industry has been another effective approach at the disposal of tobacco control advocates to raise awareness of the problem of smoking in the public eye (Chapman, 1996). Litigation has not only provided access to secret internal tobacco industry documents, it has also weakened the economic position of tobacco companies, which had to pass the costs of litigation cases on to the consumer, thus directly leading to a decrease in consumption (Daynard, 2003). In addition, litigation and the action of whistleblowers has also increased pressure on tobacco companies to show social responsibility and has raised awareness of their unethical practices by drawing negative media attention (Jacobson & Warner, 1999).

### **I.v.iii Intervention programmes**

Cessation and prevention programmes encompass a whole range of measures to curtail the tobacco epidemic - ranging from the brief advice of health professionals to the intensive, multi-session counselling of trained smoking cessation advisors. There is ample evidence for the effectiveness of brief advice provided by doctors, which has

been shown to increase quit rates by about 2% (West, McNeill, & Raw, 2000; Lancaster & Stead, 2004). While this may not seem very much, brief advice has the potential to affect population smoking prevalence because of the wide-reach of the intervention, and routine repeated advice may increase the chances of successful quitting even further (Fiore, Bailey, Cohen, Dorfman *et al.*, 2000). There is, however, less clear evidence regarding the effectiveness of brief quit advice from other professions, the specific setting or tailoring of brief advice (Stead, McNeill, Shahab, & West, 2005).

Compared with no treatment, individual, face-to-face interventions are also very effective leading to a 5-8% increase in 6-months continuous abstinence rates (Lancaster & Stead, 2005a). Success rates in group treatments are comparable, if not higher, than individual treatments (Stead & Lancaster, 2005) and have the added advantage of being more cost-effective as more smokers can be treated concurrently. Although it is clear that behavioural programmes work, especially as staff become more confident in implementing these over time (Raupach, Shahab, Neubert, Felten *et al.*, 2007), the active 'ingredient' in these types of interventions has not been isolated (West, 2006a) and particular approaches, such as cognitive behavioural therapy or motivational interviewing, have not been shown to confer additional benefits (Burke, Arkowitz, & Menchola, 2003; Stead & Lancaster, 2005; Schnoll, Rothman, Wiertel, Lerman *et al.*, 2005; Tappin, Lumsden, Gilmour, Crawford *et al.*, 2005). Indeed, the comparable success rates of interventions irrespective of the specific addenda used, from aversive smoking to self-monitoring (Shopland, Burns, Samet, & Gritz, 1991), implies that the main therapeutic impetus derives from the commonalities of these intervention (e.g. giving simple advice, building a relationship with the smoker, providing positive support), and this suggestion is supported by the effectiveness of 'buddy systems', a social support intervention, in one short-term study (West, Edwards, & Hajek, 1998)

though this effect was not repeated in a subsequent study (May, West, Hajek, McEwen *et al.*, 2006).

In addition to behavioural treatment, a plethora of medications are now available to help smokers quit. Nicotine replacement therapy (NRT) acts by replacing nicotine in the body thus alleviating withdrawal symptoms (West, Jarvis, Russell, Carruthers *et al.*, 1984) but also by providing a control or coping mechanism to deal with the behaviour change (West, 1992). NRT has been around for more than 20 years, first in the form of the nicotine gum (Brantmark, Ohlin, & Westling, 1973), and then transdermal patch (Rose, Herskovic, Trilling, & Jarvik, 1985). Over the years, nicotine lozenges, sublingual tablets, spray and inhaler have been added to the range of available NRTs. NRT has been shown to be an effective cessation aid, approximately doubling long-term abstinence (Silagy, Lancaster, Stead, Mant *et al.*, 2004). There appears to be no difference in the efficacy of various NRT products (Hajek, West, Foulds, Nilsson *et al.*, 1999); however, among more highly dependent smokers there is some evidence for a dose response relationship (Hughes, Lesmes, Hatsukami, Richmond *et al.*, 1999) and nasal spray appears to be particularly effective (Sutherland, Stapleton, Russell, Jarvis *et al.*, 1992). Moreover, combining acute *ad libitum* forms (e.g. gum) with passive delivery forms (e.g. patch) of NRT seems to result in incremental efficacy (Fagerstrom, Schneider, & Lunell, 1993; Kornitzer, Boutsen, Dramaix, Thijs *et al.*, 1995).

As determined by indirect comparison, the combination of NRT with behavioural interventions appears to have an additive rather than multiplicative effect (Silagy, Lancaster *et al.*, 2004) resulting in an increase of approximately 16% in long-term abstinence in comparison with controls (Royal College of Physicians, 2000). Due to its proven efficacy, NRT has become prescription free in the UK and can be bought over

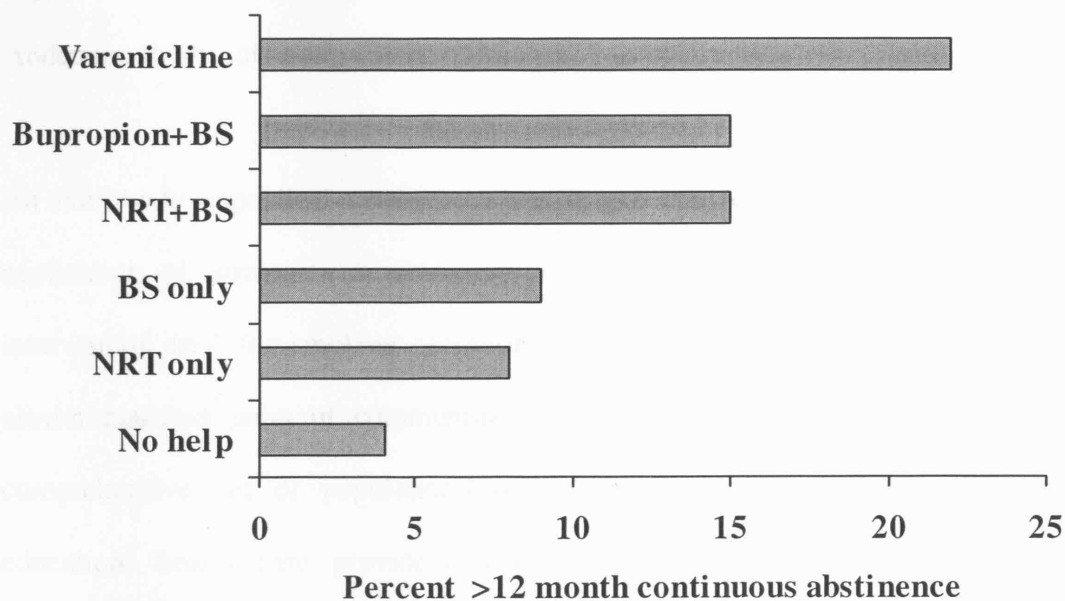
the counter in many countries (Hughes, Shiffman, Callas, & Zhang, 2003). Moreover, in the UK it has also now been licensed to be used to cut down while still smoking as well as in combination with other NRT products (Raw, McNeill, West, & Arnott, 2005).

Besides NRT, there are a number of non-nicotine pharmacological aids for smoking cessation. Of these, bupropion (amfebutamone), an antidepressant, is the most commonly used (West, 2008). It has been shown to have similar efficacy to NRT, roughly doubling quit rates (Hughes, Stead, & Lancaster, 2004), and combined therapy of bupropion with NRT significantly increases odds of abstinence compared with NRT or bupropion alone (Jorenby, Leischow, Nides, Rennard *et al.*, 1999). Nortriptyline, another antidepressant, is equally effective (Hughes, Stead, & Lancaster, 2005) but not currently licensed as a smoking cessation treatment in the UK. Both antidepressants most likely work through noradrenergic and dopaminergic action in the mid-brain by offsetting reduced activity due to nicotinic down-regulation following cessation thus lessening withdrawal effects (e.g. Roddy, 2004). In contrast to NRT, however, they have the disadvantage of causing a number of unpleasant side-effects. Another pharmacological therapy that has been extensively studied is the antihypertensive clonidine; although clonidine successfully raises long-term abstinence rates, the severe drowsiness it causes probably militates against its wide-spread use (Gourlay & Benowitz, 1995).

A very effective new pharmacological treatment is the selective partial agonist varenicline tartrate. Varenicline's particular mode of action derives from a double effect; its preferential binding to  $\alpha 4\beta 2$  nicotinic acetylcholine receptors results in moderate stimulation of the central reward pathways in the mesencephalon owing to varenicline's agonistic properties, thus relieving craving. Moreover, its blocking of the

receptor at the same time also diminishes the rewarding properties of nicotine, thus reducing the risk of a relapse (Foulds, 2006). Varenicline significantly increases cessation in comparison with both no treatment and treatment with bupropion resulting in one year abstinence rates of around 22% (Jorenby, Hays, Rigotti, Azoulay *et al.*, 2006; Oncken, Gonzales, Nides, Rennard *et al.*, 2006; Gonzales, Rennard, Nides, Oncken *et al.*, 2006). There is currently inconclusive or no evidence for the utility of other pharmacological cessation treatments including selective serotonin reuptake inhibitors, anxiolytics, opioid antagonists or nicotine vaccines (Royal College of Physicians, 2000; Covey, Sullivan, Johnston, Glassman *et al.*, 2000; Henningfield, Fant, Buchhalter, & Stitzer, 2005). Figure I.XI provides estimates of the efficacy of some of the methods discussed above in terms of their impact on 12 months continuous abstinence rates.

**Figure I.XI: Best estimate of quit rates by cessation method<sup>#</sup>**



<sup>#</sup>Data adapted from West (2006a), BS – Behavioural Support

Self-help interventions, which involve the provision of written material, quit kits or audiotapes, represent another type of smoking cessation programme and one that is very inexpensive. The effect these interventions have on cessation rates is small but significant at about 1%, and it appears that tailoring the intervention to the individual

further increases efficacy (Lancaster & Stead, 2005b) as does combining self-help with more intensive interventions (Fiore, Bailey *et al.*, 2000). Another option is the addition of newer technologies to personalise interventions by making use of the internet or mobile phones, for instance. Tailored internet-based programmes seem to have some benefit leading to increased cessation (Lenert, Munoz, Perez, & Bansod, 2004; Strecher, Shiffman, & West, 2005; Swartz, Noell, Schroeder, & Ary, 2006) and this approach may become more popular with greater access to and improvement in technology. Telephone help-lines, which - like self-help interventions and brief advice - also have the potential to reach a large number of smokers, especially when well advertised (Platt, Tannahill, Watson, & Fraser, 1997), have been demonstrated to increase cessation rates (Stead, Perera, & Lancaster, 2006); this is true in real world settings (Zhu, Anderson, Tedeschi, Rosbrook *et al.*, 2002) and when providing telephone support in addition to self-help (Miguez, Vazquez, & Becona, 2002) or NRT in trials (Zhu, Tedeschi, Anderson, Rosbrook *et al.*, 2000).

An intuitively appealing approach to smoking cessation programmes is the targeted application of strategies in community-oriented interventions. In the Community intervention trial for smoking cessation (COMMIT) one community within each of eleven matched pairs of communities in the US and Canada was allocated to a comprehensive set of population-level interventions that revolved around public education, health care providers, work-sites and cessation resources (COMMIT Research Group, 1995a). Despite the effort to engage whole communities with over 58 activities in these four different spheres of action, the analysis provided a sobering result showing that the community intervention impacted merely on mild-to-moderate but not heavy smokers, and that overall there was no significant difference in smoking prevalence between intervention and control communities (COMMIT Research Group,

1995b). Although it may be possible that specific components of the COMMIT approach were successful, in particular quit-and-win contests showed some utility (Shipley, Hartwell, Austin, Clayton *et al.*, 1995), there is very little evidence from this or other large-scale studies that community interventions appreciably reduce smoking levels (Secker-Walker, Gnich, Platt, & Lancaster, 2002). In contrast, multi-component programmes at the individual level have proven very effective – be it in special (Rigotti, Munafo, Murphy, & Stead, 2003; Anthonisen, Skeans, Wise, Manfreda *et al.*, 2005) or in general populations (Fiore, Bailey *et al.*, 2000; Dale, Ebbert, Hays, & Hurt, 2000). However, as indicated earlier, due to the complexity of interventions and presence of confounders, it is not really possible to determine whether there are specific additive or multiplicative interactions between components, and whether all, most or only some components confer an actual benefit in these intervention programmes (Piasecki & Baker, 2001).

With the ratification of the world's first health treaty in 2004 by over 40 countries, the WHO Framework Convention on Tobacco Control (FCTC) formally became international law in 2005, and there now exists a unique tool to enable the application of the various tobacco control strategies discussed here at a global level; an opportunity, which must not be missed (Wipfli, Stillman, Tamplin, da Costa e Silva VL *et al.*, 2004). Tobacco control has achieved a lot over the past decades. As Chapter II will highlight, this progress would not have been possible without the use of biological markers in nearly every area of tobacco control; by advancing our understanding of the aetiology and biology of smoking-related diseases but also by raising awareness of the impact of smoking on others, by furthering smoking cessation treatments and by providing policy makers with facts to argue from and tools to regulate with.



## Chapter II

### Smoking-related biological markers

Within the context of tobacco control, biological markers, or biomarkers for short, denote biological indices of smoking-related exposure, risk or harm (McClure, 2001) and a non-exhaustive list of examples for each of these is presented in Table II.I. A biomarker can be any agent or compound from a bodily fluid, including exhaled air, or from a bodily tissue that is directly or indirectly related to a smoke constituent (e.g. a metabolite) but biomarkers can also represent an interactive effect of these constituents with the body (e.g. tissue damage) or known mediating factors like aberrations in metabolism that potentiate these interactions (Shields, 2002). Biological markers of exposure, risk and harm play an important role in tobacco control strategies, and the various types of biomarkers will be briefly presented. However, it should be noted that, as indicated in Table II.I, it is not always possible to clearly delineate different categories of biomarkers as some can fulfil several functions at once; for instance, expired air-carbon monoxide is both a biomarker of exposure but has also been linked to disease risk and thus is represented along the continuum between exposure and risk biomarkers.

In the following section, each type of smoking-related biomarker (exposure, risk and harm) is considered in more detail and examples of each type provided to give an idea of this area of research. As outlined in Chapter I, tobacco control can be divided in three main areas of action – legislation and policy; basic research, public awareness and values; and intervention programmes – and in this Chapter the contribution of the three biomarkers types to these areas of action will also be discussed. However, since the focus of this thesis concerns the role of biomarkers in smoking cessation (that is, primarily on intervention programmes), the application of biomarkers in smoking

cessation interventions will be further evaluated in a meta-analysis in Chapter III and will therefore receive somewhat less attention in this Chapter.

**Table II.I: Biomarker class by biomarker source matrix<sup>#</sup>**

BIOMARKER SOURCE	BIOMARKER CLASS CONTINUUM		
	Exposure	Risk	Harm
Nicotine	Serum nicotine Cotinine		
Tobacco alkaloids	Anatabine Anabasine		
Carbon-monoxide	COHb Breath carbon-monoxide		
Tobacco-specific- N-nitrosamines		HPB- haemoglobin NNAL	
Polycyclic Aromatic Hydrocarbons		BPDE- haemoglobin 1-HOP	
Neuroendocrine markers		Cortisol	
Genetic markers of susceptibility		CYP, GST NAT	
DNA mutations		D-loop, <i>ND4</i> <i>p53</i> , K-ras	
Lipids		HDL LDL	
Cardiovascular response		Heart rate Blood pressure	
Cardiovascular morphology		IMT Atherosclerotic plaque	
Pre-cancerous lesions		Oral leukoplakia Squamous dysplasia	
Pulmonary Function			FEV <sub>1</sub> FVC

<sup>#</sup>Adopted from Stratton *et al.* (2001), Hecht (2003); COHb: Carboxyhaemoglobin; HPB: 4-hydroxy-1-(3-pyridyl)-1-butanone; NNAL: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; BPDE: benzo(a)pyrene-7,8-diol-9,10-epoxide; 1-HOP: 1-hydroxypyrene; CYP: cytochromes P450; GST: glutathione S-transferases; NAT: N-acetyltransferases; D-loop: displacement loop; *ND4*: nicotinamide adenine dinucleotide dehydrogenase subunit 4 gene; *p53*: tumor suppressor gene; K-ras: Kirsten-ras proto-oncogene; HDL: High density lipoprotein, LDL: Low density lipoprotein; IMT: Intima-media thickness; FEV<sub>1</sub>: Forced expiratory volume in one second; FVC: Forced vital capacity

## ***II.i Exposure biomarkers***

### ***II.i.i Range of exposure biomarkers***

Exposure biomarkers are generally obtained from analysis of exhaled air, sputum, saliva, blood, skin, hair or urine (Davis & Curvall, 1999). One of the most inexpensive and easily obtained biomarkers of exposure is expired air carbon-monoxide (CO), which is measured with commercially available breathalysers and has been shown to be a relatively good marker of smoke exposure (Jarvis, Tunstall-Pedoe, Feyerabend, Vesey *et al.*, 1987). While it is best as an estimator of recent exposure due to its short half-life (Coburn, Forster, & Kane, 1965), it has also been shown to be predictive of long-term smoking-related outcomes such as lung cancer (Law, Morris, Watt, & Wald, 1997). However, breath CO has a number of drawbacks; it is not specific to tobacco smoke as there are other tobacco unrelated sources of CO exposure such as vehicle exhaust emissions (Sonnenworth & Jarrett, 1980). In addition, physical activity, lung disease and gender can all influence CO levels, and since CO is related to combustion, it is not applicable to the detection of smokeless forms of tobacco (Benowitz, Jacob, III, Ahijevych, Jarvis *et al.*, 2002).

Instead of expired air, it is also possible to measure CO in blood (carboxy-haemoglobin), which is highly correlated with breath CO (Jaffe, Kanzler, Friedman, Stunkard *et al.*, 1981). However, this approach shares the limitation of breath CO and has the added disadvantage of being more intrusive. Another blood-based exposure biomarker is plasma nicotine, which correlates well with tobacco use (Benowitz & Jacob, III, 1984) as does urinary nicotine (Jacob, III, Yu, Shulgin, & Benowitz, 1999). However, due to the short half-life of nicotine of about 2 hours (Benowitz & Jacob, III, 1994), cotinine, the major metabolite of nicotine is more commonly used as it has a substantially longer half-life (Benowitz, Jacob, III *et al.*, 2002). Cotinine can be

measured in plasma, saliva and urine and is very reliable in terms of its sensitivity and specificity to tobacco use with the exception of NRT users (Benowitz, Kuyt, Jacob, III, Jones *et al.*, 1983).

Thiocyanate, a metabolite of hydrogen cyanide, can also be measured in plasma, saliva and urine but is only specific to heavy smoking and not light smoking due to the confounding effect of dietary sources of thiocyanate at lower levels of exposure (Swan, Parker, Chesney, & Rosenman, 1985). It also does not detect smokeless forms of tobacco use as hydrogen cyanide is a combustion product. In contrast, anatabine and anabasine, nicotine-related alkaloids present in tobacco, can detect tobacco use irrespective of the method of consumption (Jacob, III, Yu *et al.*, 1999). They have the additional advantage that unlike cotinine or other nicotine-related biomarkers they are not confounded with NRT use as these alkaloids are not present in nicotine-containing medication (Benowitz, Jacob, III *et al.*, 2002). However, as the method used to detect anabasine and anatabine involves the combination of gas chromatography and mass spectrometry, which requires trained personnel and is an expensive procedure and therefore not commonly used at the moment.

### **II.i.ii Application of exposure biomarkers in tobacco control**

Biomarkers of exposure have played an important role in establishing public awareness of passive smoking and thus in the introduction of smoke-free legislation (Howard, 2004). Exposure biomarkers, such as cotinine, have been crucial in determining environmental exposure levels of non-smokers to cigarette smoke (Jaakkola & Jaakkola, 1997); for instance, the detection of raised exposure levels among flight attendants resulted in the banning or voluntary suspension of smoking on most airplanes (Repace, 2004). Similar results have been obtained by comparing smoke exposure biomarkers of patrons (Fowles, Christophersen, Fernando, Lea *et al.*, 2006) and workers in smoky bars

(Jarvis, Foulds, & Feyerabend, 1992). The link between environmental tobacco smoke (ETS) and various smoking-related diseases (Hackshaw, Law, & Wald, 1997; Law, Morris, & Wald, 1997) has provided a powerful argument for the tobacco control community to urge for the introduction of smoke restrictions in public (Chapman & Wakefield, 2001). In addition, ETS exposure levels have been linked to sudden infant death syndrome (Rajs, Rasten-Almqvist, Falck, Eksborg *et al.*, 1997), asthma in children (Lodrup Carlsen & Carlsen, 2001) and low birth weight (Eskenazi, Prehn, & Christianson, 1995); all of which has shifted people's attitudes towards smoking reduction at home. However, more work still needs to be done in the area (Green, Courage, & Rushton, 2003).

As will be explained further in the next chapter, exposure biomarkers have also been used in smoking interventions, and there are a number of studies that have found some positive effect on smoking behaviour, including increases in cessation rates both in the general population (McClure, 2004) and among pregnant women (Cope, Nayyar, & Holder, 2003). As the reinforcing action of smoking is in part dependent on the speed of the bioavailability of nicotine (Pomerleau, 1992), the measurement of exposure biomarkers, especially venous nicotine levels, has also been important for the development and evaluation of nicotine replacement products, showing for instance that faster delivery methods of nicotine in some NRT products such as nasal spray (Henningfield, 1995) may be particularly helpful for more heavily addicted smokers as it more closely approximates the rewarding effects of cigarettes (Sutherland, Stapleton *et al.*, 1992; Lerman, Kaufmann, Rukstalis, Patterson *et al.*, 2004).

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## **II.ii Risk biomarkers**

### **II.ii.i Range of risk biomarkers**

Smoking-related risk biomarkers are manifold and like exposure biomarkers can be sampled and detected in different bodily tissues and fluids. By virtue of their function, putative risk biomarkers go beyond exposure biomarkers in that they are linked to the probable development of subsequent diseases and may already be indicators of harm (for examples see Table II.I). Among others, risk biomarkers include metabolites of smoking-related carcinogens such as tobacco-specific *N*-nitrosamines (TSNA) and polycyclic hydrocarbons (PAH) as well as genetic markers of susceptibility, which have all been related to disease outcomes (Hoffmann, Djordjevic *et al.*, 1997; Au, Oh, Grady, Salama *et al.*, 2001; Hecht, 2002a; Hecht, 2003).

As discussed in Chapter I, the most common illnesses among smokers are neoplastic, non-cancerous respiratory or cardiovascular diseases, and markers of PAH and TSNA exposure as well as genetic markers play an important role for the prediction of risk to develop these diseases. The carcinogenicity of PAH has been comprehensively proven by both animal and human research (International Agency for Research on Cancer, 1986, 2004). Hydrocarbons such as benzo[a]pyrene (BaP) are metabolised to diol and phenol epoxides, which react with DNA to form adducts (Cooper, Grover, & Sims, 1983). DNA adduct formation is a crucial step in carcinogenesis (Phillips, 2002) and significant associations between PAH-related DNA adduct levels (such as benzo(a)pyrene-7,8-diol-9,10-epoxide (BPDE) adducts) and cancer in smokers' tissue has been reported (Kriek, van Schooten, Hillebrand, Van Leeuwen *et al.*, 1993; Kriek, Rojas, Alexandrov, & Bartsch, 1998; but also see Godschalk, van Schooten, & Bartsch, 2003). PAHs, and BaP in particular, have also been demonstrated to cause cardiovascular damage in animals (Ramos, Zhang, Sadhu, & Chapkin, 1996) and

humans (Vayssier-Taussat, Camilli, Aron, Meplan *et al.*, 2001) by inducing necrosis and formation of oxidative metabolites.

TSNAs have been equally implicated in disease risk (Hoffmann, Brunnemann, Prokopczyk, & Djordjevic, 1994). For instance, the nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and its metabolite NNAL (see Table II.I) are involved in lung (Foiles, Akerkar, Carmella, Kagan *et al.*, 1991) and pancreatic carcinogenesis (Rivenson, Hoffmann, Prokopczyk, Amin *et al.*, 1988) through the alkylation of DNA bases and the formation of DNA adducts (Hecht, Carmella, Foiles, & Murphy, 1994); a similar process is involved in the formation of DNA adducts by  $\alpha$ -hydroxylation of *N'*-nitrosonornicotine (NNN), another nitrosamine, which has been linked to oesophageal and nasal cancer (Hecht, 1998).

The genes most relevant to smoking-related diseases are those that are involved in the xenobiotic metabolism of smoke constituents such PAHs and TSNAs (Wu, Zhao, Suk, & Christiani, 2004). The enzymes of the gene 'superfamily' cytochrome P450 (CYP) convert many tobacco carcinogens into DNA-binding metabolites and can thus modulate the risk for cancer (Bartsch, Nair, Risch, Rojas *et al.*, 2000). Polymorphisms of CYP genes *CYP2A6*, *CYP1A1* and *CYP2D6* have been associated with the development of smoking-related cancers, such as lung cancer (Taioli, Gaspari, Benhamou, Boffetta *et al.*, 2003), oral cancer (Sato, Sato, Izumo, & Amagasa, 1999) and breast cancer (Ambrosone, Freudenheim, Graham, Marshall *et al.*, 1995); however, results in this area have been somewhat inconsistent (Bartley & Plewis, 1997; London, Idle, Daly, & Coetzee, 1999).

Glutathione S-transferase (GST) enzymes belong to another gene 'superfamily' and are involved in detoxifying smoking-related carcinogens such as PAHs (Rebbeck, 1997). Deficiency of GST genes (*GSTM1* in particular) has been linked to increased lung cancer risk (Houlston, 1999; Benhamou, Lee, Alexandrie, Boffetta *et al.*, 2002) and bladder cancer (Engel, Taioli, Pfeiffer, Garcia-Closas *et al.*, 2002). GST genes have also been associated with cardiovascular disease risk (Li, Boerwinkle, Olshan, Chambless *et al.*, 2000; Olshan, Li, Pankow, Bray *et al.*, 2003) but there is some contradictory evidence (Van Schooten, Hirvonen, Maas, De Mol *et al.*, 1998). In addition, in a number of case control studies both *GSTM1* and *GSTP1* (another GST family gene) were shown to be significantly associated with respiratory illnesses such as COPD (Baranova, Perriot, Albuissou, Ivaschenko *et al.*, 1997; He, Connett, Anthonisen, Pare *et al.*, 2004) but again findings are inconsistent (Silverman, 2006).

N-acetyltransferase (NAT) genes are the last of the 'superfamilies' of genes primarily involved in the metabolism of carcinogens (Thier, Bruning, Roos, Rihs *et al.*, 2003). Of these both the *NAT1* and *NAT2* genotype have been linked to smoking-related bladder cancer risk (Kadlubar & Badawi, 1995; Inatomi, Katoh, Kawamoto, & Matsumoto, 1999; Vineis, Marinelli, Autrup, Brockmoller *et al.*, 2001) and, in the case of *NAT1*, potentially to gastric (Gonzalez, Sala, & Capella, 2002) and lung cancer risk (Abdel-Rahman, El-Zein, Zwischenberger, & Au, 1998), respectively. Beyond markers of an individual's genetic risk, there is also evidence that biomarkers which measure chromosome alterations that are caused by smoking-related constituents (and in this sense are both risk and harm biomarkers) predict subsequent disease (Stratton, Shetty *et al.*, 2001).



As discussed above, PAHs and TSNA are responsible for the formation of DNA adducts; these are usually removed by a variety of repair systems to return chromosomes to their normal state (Norbury & Hickson, 2001), but if adducts persist, mutations may ensue (Goode, Ulrich, & Potter, 2002). When mutagenic effects occur in functionally important regions of mitochondrial or chromosomal DNA, such as areas responsible for replication (e.g. d-loop), oxidative phosphorylation genes (e.g. *ND4*), proto-oncogenes (e.g. K-ras) or tumor suppressor genes (e.g. *p53*), this may increase cancer risk (Fliss, Usadel, Caballero, Wu *et al.*, 2000; Osada & Takahashi, 2002). Resultant DNA lesions can be assessed with a number of techniques including cytogenetics (Ramsey, Moore, Briner, Lee *et al.*, 1995) and polymerase chain reaction methods that measure loss of heterozygosity (Mao, Lee, Kurie, Fan *et al.*, 1997); the efficacy of this approach is supported by evidence showing that such damage has been shown to predict actual occurrence of cancer in the general population (Hagmar, Brogger, Hansteen, Heim *et al.*, 1994).

Besides genetic markers of smoking-related risk, there also exist various neuro-endocrine markers that are associated with smoking. Smoking has a consistent effect on hormone secretion including the hypothalamic-pituitary-adrenal (HPA) axis (Kapoor & Jones, 2005), which is important for the body's response to physical as well as mental stressors (Miller & O'Callaghan, 2002). A relatively reliable marker of HPA axis activation when measured throughout the day is the peripheral concentration of cortisol, which can easily be assessed in saliva and has been shown to be elevated in smokers throughout the day (Kirschbaum, Wust, & Strasburger, 1992; Baron, Comi, Cryns, Brinck-Johnsen *et al.*, 1995; Badrick, Kirschbaum, & Kumari, 2007) as well as to decrease with smoking cessation (Ussher, West, Evans, Steptoe *et al.*, 2006). Since activation of the HPA axis (and thus raised cortisol) is indicative of low grade

inflammation, which is likely to result from exposure to smoke constituents, it has been suggested as a causal factor in the aetiology of various smoking-related diseases including osteoporosis and heart disease (Manelli & Giustina, 2000).

Another group of risk biomarkers that has been extensively studied in relation to both smoking and cardiovascular diseases are lipids (Muscat, Harris, Haley, & Wynder, 1991) and cardiovascular response (Samuelsson, 1988). Smoking is known to influence high (HDL) and low density lipoprotein (LDL) levels in plasma (Craig, Palomaki, & Haddow, 1989; Wilson, 1990), which in turn has been clearly associated with coronary disease (Stampfer, Sacks, Salvini, Willett *et al.*, 1991; Kinosian, Glick, & Garland, 1994). Moreover, smoking cessation and reduction is associated with an improvement in lipid levels (Eliasson, Hjalmarson, Kruse, Landfeldt *et al.*, 2001; Hatsukami, Kotlyar, Allen, Jensen *et al.*, 2005). In contrast, although a tentative causal relationship between smoking and cardiovascular responses such as hypertension and raised blood pressure has been suggested (Sleight, 1993; Kochar & Bindra, 1996), there is currently not enough evidence to confirm this proposition (Green & Harari, 1995). However, there exists good evidence for the interaction between smoking and cardiovascular response and eventual cardio-vascular disease (CVD), and this is underlined by the protective influence of cessation on subsequent coronary disease in the presence of hypertension (Samuelsson, 1988; Zanchetti, Hansson, Dahlof, Elmfeldt *et al.*, 2001; Almgren, Persson, Wilhelmsen, Rosengren *et al.*, 2005). These risk biomarkers, which - by virtue of their evidencing damaging changes in biological parameters - are also biomarkers of harm, have the added advantage that they are easily and inexpensively assessed in contrast to other risk biomarkers (Stratton, Shetty *et al.*, 2001).

### **II.ii.ii Application of risk biomarkers in tobacco control**

The most obvious application of risk biomarkers is in research and in furthering our insights into the pathogenesis of diseases that are associated with smoking. For instance, biomarkers of oxidation have helped to establish the influence of smoking in vascular injury (Chehne, Oguogho, Lupattelli, Budinsky *et al.*, 2001), and genetic biomarkers have helped our understanding of the differential development of tobacco-related cancers in smokers (Bartsch, Nair *et al.*, 2000; Benhamou, Lee *et al.*, 2002) and non-smokers (Bennett, Alavanja, Blomeke, Vahakangas *et al.*, 1999). Moreover, the increase in HPA axis activity (a measure of stress) that is caused by smoking may help explain the association of smoking with mental disorders (Steptoe, Wardle, & Marmot, 2005). The evidence from risk biomarkers, which have provided proof of plausible pathways between smoking and diseases is important for several reasons. It corroborates hitherto suspected but thus far only indirectly inferred causal association between smoking and diseases<sup>7</sup>, which may not only reinforce the health message - thus raising public awareness - but also strengthen the legislative case of policy makers (Phillips, 2002). In addition, risk biomarkers are also crucial for advances in the first-line treatment of smoking-related diseases as shown by the case of TSNA biomarkers, which may prove useful for the development of cancer chemoprevention (Hecht, 1997).

Yet, possibly the most important role for risk biomarkers lies in their application to product regulation and harm reduction (Shields, 2002; Hecht, 2002b). While smoking cessation may be the ideal end-point for any tobacco control approach, it is clear that for many smokers this outcome is not attainable, and harm reduction - by permanently

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<sup>7</sup> In the case of cancer, for instance, the tobacco industry for a long time publicly denied any link between smoking and lung cancer as most early studies were epidemiological and therefore did not prove a 'causal' link between smoking and cancer; a spurious argument which was arguably nullified through evidence of direct biological causation espoused by risk biomarkers such as *p53* (Parascandola, 1998; Parascandola, 2004)

switching to different products like 'potential reduced exposure products' (PREPs) or NRT - may be the next best thing (Hatsukami, Henningfield, & Kotlyar, 2004). However, in order to evaluate harm reduction strategies, it is crucial to determine if they actually lower the dose of carcinogens and other biologically detrimental metabolites by using biomarkers (Stratton, Shetty *et al.*, 2001). Although we do not currently know what dose of reduction leads to reduction in measurable disease incidence, clinical studies involving biomarkers present a first step in the right direction until epidemiological studies can provide definitive data (Hatsukami, Giovino, Eissenberg, Clark *et al.*, 2005). Early studies, for instance, have shown that reduction of smoking in conjunction with NRT-use does not lead to reductions in risk biomarkers such as NNAL (Hurt, Croghan, Wolter, Croghan *et al.*, 2000) or malondialdehyde, a biomarker of oxidative stress (Petruzzielli, Tavanti, Pulera, Fornai *et al.*, 2000); neither does a switch to PREPs such as OMNI cigarettes (Hughes, Hecht, Carmella, Murphy *et al.*, 2004). In contrast, switching from other smokeless forms of tobacco to Swedish snus has been shown to reduce nitrosamine levels (Hatsukami, Lemmonds, Zhang, Murphy *et al.*, 2004).

A related and equally novel topic in product regulation concerns the utility of risk biomarkers in determining the exposure to harmful constituents in existing products. Since the 1960s commercially available cigarettes have been tested by machine-smoking regimes to determine the toxicity of cigarettes, either according to U.S. Federal trade commission (FTC) or to largely similar International Organisation for Standardization (ISO) specifications (Kozlowski & O'Connor, 2002). However, these smoking regimes are problematic since the applied puffing parameters clearly misrepresent human smoking: smokers tend to take greater puffs, inhale more deeply and frequently and block ventilation holes (Djordjevic, Hoffmann, & Hoffmann, 1997).

Smokers also compensate by smoking low-tar cigarettes more intensely to obtain relatively consistent levels of nicotine from cigarettes and this behaviour has completely negated any positive health impact of so called 'light' cigarettes (Augustine, Harris, & Wynder, 1989; Kozlowski & O'Connor, 2002). Indeed, cigarettes have been purposefully designed to produce lower constituents yields when machine-tested than when smoked under realistic conditions (Hammond, Collishaw, & Callard, 2006) and to rectify the problems of the FTC/ISO method, new and more intensive testing regimes have been proposed and, in Canada, already implemented (Kozlowski & O'Connor, 2000). Risk biomarkers have been helpful in identifying the differences between human and machine smoking (Djordjevic, Stellman, & Zang, 2000; Hecht, Murphy, Carmella, Li *et al.*, 2005) and as ISO is reconsidering its current smoking regime, a pressing task within product regulation will be to determine which, if any, potential smoke testing regime best represents human smoking behaviour (Hammond, Fong, Cummings, O'Connor *et al.*, 2006). Biomarkers are crucial for this process by allowing for the comparison of machine smoke yields (e.g. NNK) with corresponding levels of carcinogens intake in humans (e.g. NNAL).

Following recent advances in technology, risk biomarkers, and especially markers of genetic susceptibility, have also become more popular as an addendum to smoking cessation interventions and this aspect of their application in tobacco control will be discussed in more detail in the next chapter. However, the results of studies using risk biomarkers have been somewhat mixed. For instance, one study which provided feedback on lipids as a biomarker of coronary risk found no increase in smoking cessation rates but changes in other health behaviours such as alcohol consumption and diet (Hanlon, McEwen, Carey, Gilmour *et al.*, 1995). Altogether then, it would appear

that there remain untapped opportunities for the application of risk biomarkers in intervention programmes.

### ***II.iii Harm biomarkers***

#### **II.iii.i Range of harm biomarkers**

The last group of biomarkers to be considered are harm biomarkers, which are indices of smoking-related harm measurable in general human physiology, including respiratory physiology, immunology and pathophysiology. While harm biomarkers like risk biomarkers may be indicative of disease, these biomarkers by themselves also evidence actual harm caused by smoking. Yet, as a caveat it should be noted that most of the harm biomarkers that will be described are not necessarily specific to smoking alone (e.g. unfavourable lipid levels can occur in non-smokers, too) but rather these harm biomarkers have also been explicitly associated with smoking. Moreover, owing to the overlap between risk and harm biological markers (see Table II.I), some of the biomarkers that have been mentioned in the previous section could also have been included here. However, as there is a plethora of possible harm biomarkers, and in the interest of parsimony, only a selection relevant to each of the most common illnesses among smokers (cardiovascular, neoplastic and non-malignant pulmonary diseases) will be discussed in this section.

Atherosclerosis is thought to be the underlying pathology in most cases of cardiovascular diseases (Cowie, 2004). In atherosclerosis smooth muscle cells proliferate and fatty substances, in particular cholesterol and triglycerides, accumulate in the walls of arteries (Tortora & Grabowski, 2002). This leads to the thickening of the intima-media and eventually to the formation of atherosclerotic plaque, which - as it grows - obstructs blood flow in the affected artery (Kadar & Glasz, 2001). In addition,

plaque can also cause the formation of an embolus (clot transported by blood) that may obstruct smaller arteries and capillaries downstream from the site of formation (Davies & Thomas, 1985; Ambrose, Tannenbaum, Alexopoulos, Hjemdahl-Monsen *et al.*, 1988). For these reasons, atherosclerosis is assumed to be one of the principle causes of CVDs such as myocardial infarction and coronary artery disease (Tofler & Muller, 2006), and CVD will be discussed in more detail in Chapter IX.

Smoking is involved in the pathogenesis of atherosclerosis in multiple ways (McGill, Jr., 1990; Chia & Newby, 2002). It causes arterial endothelial cell damage and increases plasma cholesterol and low-density lipoproteins, while decreasing high-density lipoproteins (Brischetto, Connor, Connor, & Matarazzo, 1983), which leads to the development of plaque. It may also influence the cellular immune system and promote aberrant expression of DNA resulting in cellular hyperplasia (Barrett & Benditt, 1988) as well as affecting plasma coagulation pathways and a number of other factors involved in the progress of atherosclerosis (Diana, 1990). As plaque and intima-media thickness (IMT) can be demonstrated non-invasively and relatively easily with standard ultrasound transducers (Wendelhag, Gustavsson, Suurkula, Berglund *et al.*, 1991; Veller, Fisher, Nicolaides, Renton *et al.*, 1993; el-Barghouti, Elkeles, Nicolaides, Geroulakos *et al.*, 1997), they are ideal biomarkers of harm for CVD.

In terms of lung cancer, there are a number of pre-invasive lesions including squamous dysplasia, carcinoma in situ and atypical adenomatous hyperplasia that indicate smoking-related pulmonary harm, which have predictive value for lung cancer development but are not themselves considered to be lung cancer (Kerr, 2001). The causal role of smoking in pre-neoplastic changes in the lung has been shown both in animal models (Thomassen, Chen, Mauderly, Johnson *et al.*, 1989) and humans

(Wistuba, Mao, & Gazdar, 2002) and is most likely triggered by DNA damage (Belinsky, Nikula, Palmisano, Michels *et al.*, 1998). While screening for lung cancer using sputum examination, chest radiography and computer tomography has not been shown to decrease lung cancer mortality (Manser, Irving, Byrnes, Abramson *et al.*, 2003) with recent advances in technology there are now new techniques available to image lesions previously not detectable (Rossi, Maione, Colantuoni, Gaizo *et al.*, 2005), for instance by using fluorescence bronchoscopy (Lam, MacAulay, Hung, LeRiche *et al.*, 1993; George, 1999). Although there is some doubt about the specificity of this particular technique (Kurie, Lee, Morice, Walsh *et al.*, 1998), other methods such as bronchovideoscopy show promise in improving the reliable detection of pre-cancerous lung tissue even further (Shibuya, Hoshino, Chiyo, Iyoda *et al.*, 2003).

Another neoplasm clearly linked to tobacco use and smoking is cancer of the mouth (Blot, McLaughlin, Winn, Austin *et al.*, 1988; Mashberg, Boffetta, Winkelman, & Garfinkel, 1993; Johnson, 2001) and precancerous oral tissue can provide another set of potential biomarkers. For example, leukoplakia denotes white - and erythroplakia red - lesions in the oral cavity, which are identifiable with the naked eye and linked to the development of oral cancer (Neville & Day, 2002). These oral lesions like other mutations in buccal pre-cancerous cells are associated with tobacco use (Proia, Paszkiewicz, Nasca, Franke *et al.*, 2006). Changes in buccal cells can be identified by fluorescence spectroscopy (de Witjes, Sterenberg, & Roodenburg, 2005; Sharwani, Jerjes, Salih, Macrobert *et al.*, 2006) or tissue dyes like toluidine blue that stain oral premalignant lesions (Onofre, Sposto, & Navarro, 2001; Zhang, Williams, Poh, Laronde *et al.*, 2005) thus increasing their early detection (Bsoul, Huber, & Terezhalmay, 2005). While the incidence of false positives can be high, changes in protocol have been shown



to improve the specificity of these approaches thus indicating utility for screening (Mashberg, Boffetta *et al.*, 1993).

Smoking is a well established risk factor for non-cancerous pulmonary diseases such as COPD (Anto, Vermeire, Vestbo, & Sunyer, 2001; Calverley & Walker, 2003). Chronic obstructive pulmonary disease (also known as chronic obstructive airways or chronic obstructive lung disease) will be discussed further in Chapter VIII and is defined as a largely irreversible airflow obstruction that does not change appreciably over a number of months (Lomas, 2002) and therefore really includes a range of conditions such as emphysema and chronic bronchitis (Rennard, 1998). Although its diagnosis is in part prompted by evidence of symptoms such as chronic cough, sputum or dyspnoea, the machine assessment of air lung capacity through spirometry is considered the gold standard (Pauwels, Buist, Calverley, Jenkins *et al.*, 2001). Among other measures, spirometry determines forced vital capacity (FVC) - the volume of air exhaled during maximal expiration - as well as the forced expiratory volume in one second (FEV<sub>1</sub>), both of which function as indicators of damage to the lung (Celli & MacNee, 2004). These harm biomarkers predict COPD-related morbidity and mortality (Fletcher & Peto, 1977; Peto, Speizer, Cochrane, Moore *et al.*, 1983) and enable the detection of early stages of the disease, which may help reduce the burden of COPD by instigating behaviour change (Wilson, Adams, Appleton, & Ruffin, 2005; Leff, 2005).

### **II.iii.ii Application of harm biomarkers in tobacco control**

Harm biomarkers have been essential in raising awareness of smoking-related diseases in the population through the publications of biomarker-related discoveries in the literature. From the Framingham Heart studies, which provided clear evidence of the harmful effects of smoking on cardiovascular markers (Kannel, Wolf, Castelli, & D'Agostino, 1987; Freund, D'Agostino, Belanger, Kannel *et al.*, 1992), via the Lung

Health Study proving the benefits of cessation on lung function markers (Anthonisen, 2004), through to studies showing a causal link between smoking and biomarkers of ocular harm such as cataracts and macular degeneration (DeBlack, 2003) and investigations evidencing the harmful effects of tobacco use on markers of reproductive health (Vine, 1996; Lyons, Saridogan, & Djahanbakhch, 2006), harm biomarkers have been invaluable utensils in the tobacco control tool box.

In the case of product regulation, harm biomarkers have been incorporated into new legislation as part of the Framework Convention on Tobacco Control (FCTC), which provides for the introduction of visual warning labels evidencing smoking-related harm on cigarette packs (Joossens, 2000). The tobacco industry has long been lobbying against the introduction of warning labels but despite their efforts, graphic warning labels have already been implemented in countries such as Australia, Brazil, Canada and Malaysia (Chapman & Carter, 2003; Swanson, 2006). The use of graphic images depicting harm caused by smoking is supported by theoretical considerations; imagery more readily allows for the spanning of the conscious-unconscious continuum than overt or covert language and it is therefore less likely to be filtered through the conscious critical apparatus (Horowitz, 1970) and thus more likely to impact directly on information and emotional processing. Imagery affords a greater capacity than the linguistic mode for both the attraction and focusing of emotionally loaded associations (Sheikh & Jordan, 1983) and cognitive processing in general (Hitch & Baddeley, 1976). Cognitive performance increases with imageability of material as items are increasingly likely to be stored in both verbal and non-verbal codes (Marschark & Hunt, 1989). In agreement with these suggestions, it has indeed been found that graphic warning labels improve recall, increase depth of processing (Hammond, Fong *et al.*, 2003) and improve communication of health risks (Hammond, Fong, McNeill, Borland *et al.*, 2006), thus

leading to an increase in cessation-related cognitions and actions (Hammond, McDonald, Fong, Brown *et al.*, 2004; Potschke-Langer & Schulze, 2005; O'Hegarty, Pederson, Nelson, Mowery *et al.*, 2006).

Indeed, for the same reasons that favoured the introduction of graphic health warnings, harm biomarkers have been advocated in smoking cessation programmes in order to make health promotion communication more salient (Lerman, Orleans, & Engstrom, 1993). Thus far, harm biomarkers for a relatively small number of diseases have been incorporated in smoking cessation interventions (McClure, 2001) and Chapter III will systematically analyse their impact on cessation and other outcomes. For instance, both spirometry for COPD and CT scans for lung cancer have been used as an addition to smoking cessation interventions. While the former has produced rather mixed results (Badgett & Tanaka, 1997), there is some evidence that supports the use of CT scanning for lung cancer as a motivator in smoking cessation interventions by virtue of the fact that smokers who have abnormal scan results are both more motivated and more likely to stop smoking (Ostroff, Buckshee, Mancuso, Yankelevitz *et al.*, 2001; Cox, Clark, Jett, Patten *et al.*, 2003; Townsend, Clark, Jett, Patten *et al.*, 2005). However, despite these encouraging results, since CT scanning itself is linked to an excess increase in lung cancer risk, CT screening may not result in a decrease in lung cancer mortality and other methods may need to be pursued (Brenner, 2004).

Harm biomarkers, which may hold a better promise for the future are markers of carotid morphology since in contrast to lung cancer screening, imaging plaque or IMT has the advantage that cardiovascular effects on health are not immutable and that these harmful effects can be reversed or stopped as shown by reduced CVD mortality after smoking cessation (Raitakari, Adams, McCredie, Griffiths *et al.*, 1999; Joseph & Fu, 2003). This

approach to smoking cessation may therefore merit particular attention (Wiggers, Smets, de Haes, Peters *et al.*, 2003).

This chapter has provided an overview of smoking-related biomarkers in general and of their utilisation in various tobacco control strategies. It should be acknowledged that since the range of potential biomarkers is considerable, this discussion cannot be exhaustive. However, as this thesis focuses on the role of biological markers in smoking cessation, a more systematic analysis of their role in smoking cessation interventions is required. For this reason, the meta-analysis in Chapter III will specifically look at the evidence for the application of smoking-related biomarkers in intervention programmes to evaluate their effectiveness for changing smoking behaviours.

## Chapter III

# A systematic review and meta-analysis of the use of biomarkers in smoking cessation interventions

### *III.i Introduction*

As outlined in Chapter I, smoking prevalence has fallen considerably over the previous decades, especially so in western democratic market economies such as the UK. However, when considering that 70 to 80% of smokers would like to quit and one third have made at least three serious quit attempts, the fact that less than half of smokers achieve abstinence in their lives (World Health Organization, 1998) underlines the need for the development of new methods that prevent people from starting to smoke, motivate smokers to quit smoking and sustain long-term cessation.

There is no question that over the last decades considerable progress has been made in tobacco control. However, the progress made in smoking interventions has been relatively slow due to both the powerful addictive nature of nicotine, which has been compared to that of heroin and cocaine (e.g. Centers for Disease Control and Prevention, 1988) as well as the continuing widespread social acceptance of this behaviour. Under these circumstances, it comes as no surprise that the results offered by large-scale population-based smoking trials have been somewhat discouraging (Shiffman, 1993) and that there are calls for more and better efforts to overcome this perceptible lack of innovation (pharmacological treatments aside) in cessation strategies (Piasecki & Baker, 2001).

It has been suggested that more individualised smoking-cessation programmes may be required to enhance motivation to quit and lead to cessation among smokers (West &

Grunberg, 1991). Indeed, multi-component and self-directed interventions that are proactively delivered tend to be more successful in promoting smoking cessation than less intensive interventions (Curry, 1993; Rigotti, Munafo *et al.*, 2003; but see Lancaster & Stead, 2005a). These interventions personalise risk, they increase attention and stimulate smokers to participate in cessation programmes; in particular, providing feedback about the biological markers of smoking-related harm, risk or exposure has been suggested to motivate and reinforce quit attempts (Lerman, Orleans *et al.*, 1993). The scope of biomarkers has been explored to some degree in Chapter II, and Chapter VII provides more background regarding the rationale for offering biomarker feedback in smoking cessation interventions. Briefly, biological markers provide biological indices of smoking-related harm (e.g. reduced lung function), exposure (e.g. cotinine) or susceptibility to increased smoking-related disease risk (e.g. genetic markers). Their inclusion in cessation programmes has been proposed on the basis of theoretical considerations: to simply tell people they are at risk of developing a disease is rarely sufficient to change behaviour (Leventhal, Benyamini, Brownlee, Diefenbach *et al.*, 1997). In contrast, providing people with concrete evidence of exposure, susceptibility or harm may initiate or help maintain changes in smoking behaviour (McClure, 2004).

However, while public health demands and theoretical reflection may support the utilisation of biomarkers in cessation programmes, it remains to be seen whether this is justified in practice. The field of biomedical risk assessment is evolving (e.g. Perera & Weinstein, 2000) and this chapter aims to update two earlier reviews that have looked at this issue but arrived at somewhat contradictory conclusions: one supporting the use of biomarkers in smoking cessation (McClure, 2001) and the other not (Bize, Burnand, Mueller, & Cornuz, 2005). This meta-analysis, broadly following Cochrane review guidelines (Higgins & Green, 2005), will therefore systematically compare and evaluate

studies which have investigated the effectiveness of smoking cessation interventions that included biomarkers.

### **III.i.i Aims**

Specifically, this review will address the following questions:

- 1) Do cessation programmes enhanced with biomarker feedback improve outcome, i.e. quit rates, when contrasted with a control condition and is this effect sustainable?
- 2) What, if any, differences exist between the effectiveness of different types or combinations of biomarkers?
- 3) Which, if any, variables moderate the effect of biological markers on cessation?
- 4) What recommendations can be derived for the development of future smoking cessation programmes?

### **III.ii *Methodology***

#### **III.ii.i Study Selection**

The topic of this review required two particular restrictions on the selection of studies. Due to the advances over the recent years in the development of biological markers, their efficacy and reliability, a strict timeframe was chosen. Also, in order to obtain a minimal quality standard, which is required to capture reliably the subtle effects that are the focus of this review, only studies that were randomised controlled trials (RCT) were included<sup>8</sup>.

##### **III.ii.i.i Inclusion criteria:**

- Articles published and written in English
- Studies conducted in the past 25 years
- RCT design

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<sup>8</sup> Randomised Control Design avoids biases, which distort effects in either direction (Kleijnen, Gotzsche, Kunz, Oxman *et al.*, 1997) as both known and unknown determinants of outcome are on average evenly distributed between intervention and control groups

- At least one month follow-up
- Enrolled participants are current smokers (not ex-smokers)
- Primary outcome is behavioural, i.e. cessation of smoking
- Main focus of study is investigation of the effects of biomarker feedback on smoking cessation, which includes at least one measure of harm, exposure or susceptibility

### **III.ii.i.ii Exclusion criteria:**

- Review articles
- Observational studies
- Multiple follow-up studies that use data from the same cohort of participants<sup>9</sup>
- Intervention studies, which employed biological markers for the sole purpose of verifying smoking status not to increase cessation
- Intervention studies looking at biomarker feedback from next of kin
- Studies in which effect of biomarker feedback cannot be isolated from additional interventions provided

### **III.ii.ii Data source and search strategies**

Literature relevant to the research questions of this review was sought using three methods:

- a) Search of computerised Databases – the electronic resources used were Medline (1982 – 2007/10), Embase (1982 – 2007/09), PsycINFO (1982 - 2007/10) and ISI Web of Science<sup>®</sup> (SCI, SSCI, AHCI; 1982 - 2007). The search was carried out in October 2007. Study inclusion and exclusion terms were combined with generic (e.g. “smoking cessation”) as well as specific search terms (e.g. “biomarker\*”). The search terms were free text, not MeSH terms, to be as

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<sup>9</sup> Studies reporting a greater treatment effect are more likely to be duplicated, and inclusion of duplicated data in reviews would thus lead to bias in the estimation of effectiveness (Tramer, Reynolds, Moore, & McQuay, 1997)



inclusive as possible. The suitability of studies was initially assessed by reading abstracts, which yielded a total of 17 studies. Thereafter, the articles were further scrutinised on the basis of the full-text to determine whether they were appropriate; this identified eight suitable studies. Table III.I presents a breakdown of the search results.

**Table III.I Search History**

Data Base	Search terms			All Searches
	Smoking cessation + feedback + (see below)	Biomarker* or biological marker*	Spirometr* or CO or cotinine	Risk, harm or exposure
EMBASE	10	22	51	83
MEDLINE	9	11	31	51
Web of Science	11	17	47	75
PsycINFO	6	13	19	38
Total ( adjusted for duplicates )	12	26	78	116
Initial Selection	6	4	7	17
Final Selection	4	3	1	8

- b) Bibliography search – this search method was employed in order to identify studies, which were not picked out by the relevant search terms or are not listed on common databases<sup>10</sup>. The bibliography search of relevant articles and reviews located two further studies, which fulfilled the selection criteria.
- c) Search of meta-analyses – this search method was used to ensure that studies identified in earlier comprehensive reviews but not retrieved through methods a) or b) were included. The search of existing meta-analyses in the area produced four more studies suitable for inclusion in this review.

<sup>10</sup> According to recent research a simple search identifies approximately 42% of studies, a complex search 65% and a Cochrane high sensitivity and specificity search only about 80% of published search-relevant studies (Hopewell, Clarke, Lusher, Lefebvre *et al.*, 2002)

The final fourteen papers, which passed the selection criteria, are listed below:

- 1) Audrain, J., Boyd, N.R., Roth, J., Main, D., Caporaso, N.E. & Lerman, C. (1997). Genetic susceptibility testing in smoking cessation treatment: One year outcomes of a randomised trial.
- 2) Barnfather, K.D., Cope, G.F., & Chapple, I.L. (2005). Effect of incorporating a 10 minute point of care test for salivary nicotine metabolites into a general practice based smoking cessation programme: randomised controlled trial.
- 3) Bovet, P., Perret, F., Cornuz, J., Quilindo, J. & Paccaud, F. (2002). Improved smoking cessation in smokers given ultrasound photographs of their own atherosclerotic plaques.
- 4) Burling, T.A., Bigelow, G.E., Robinson, J.C. & Mead, A.M. (1991). Smoking during pregnancy: reduction via objective assessment and directive advice.
- 5) Cope, G.F., Nayyar, P. & Holder, R. (2003). Feedback from a point-of-care test for nicotine intake to reduce smoking during pregnancy.
- 6) Ito, H., Matsuo, K., Wakai, K., Saito, T., Kumimoto, H., Okuma, K., Tajima, K., & Hamajima, N. (2006). An intervention study of smoking cessation with feedback on genetic cancer susceptibility in Japan.
- 7) Jamrozik, K., Vessey, M., Fowler, G., Wald, N., Parker, G., & Van, V.H. (1984). Controlled trial of three different antismoking interventions in general practice.
- 8) Richmond, R.L. & Webster, I.W. (1985). A smoking cessation programme for use in general practice.
- 9) Risser, N.L. & Belcher, D.W. (1990). Adding spirometry, carbon monoxide, and pulmonary symptom results to smoking cessation counselling.
- 10) Sanders, D., Fowler, G., Mant, D., Fuller, A., Jones, L., & Marzillier, J. (1989). Randomized controlled trial of anti-smoking advice by nurses in general practice.
- 11) Segnan, N., Ponti, A., Battista, R.N., Senore, C., Rosso, S., Shapiro, S.H., & Aimar, D. (1991). A randomized trial of smoking cessation interventions in general practice in Italy.
- 12) Shahab, L., Hall, S., & Marteau, T. (2007). Showing smokers with vascular disease images of their arteries to motivate cessation: A pilot study.
- 13) Sippel, J.M., Osborne, M.L., Bjornson, W., Goldberg, B., & Buist, A.S. (1999). Smoking cessation in primary care clinics.
- 14) Walker, W.B. & Franzini, L.R. (1985). Low-Risk Aversive Group Treatments, Physiological Feedback, and Booster Sessions for Smoking Cessation.

### III.ii.iii Data extraction and analysis

As data extraction is prone to human error and may also require subjective judgement, the selected studies were reviewed using a data extraction sheet, which is provided in Appendix III.I. The form had been developed by myself prior to the review based on Cochrane specifications and was modified according to the review questions. This

practice has been shown to minimise bias when coding and rating primary studies (e.g. L'Abbé, Detsky, & O'Rourke, 1987).

Results were analysed looking at risk difference<sup>11</sup>, which arguably provides more complete and intuitive information than other measures of intervention impact such as odds or risk ratios (Laupacis, Sackett, & Roberts, 1988). The level of heterogeneity between study outcomes was assessed using that  $I^2$  statistic, which is based on Cochrane's  $Q$  but is more robust and thus suitable for smaller meta-analyses such as this (Higgins, Thompson, Deeks, & Altman, 2003). If appropriate, studies of similar methodology were pooled with the Mantel-Haenzel method using a fixed model. As suggested by the Cochrane collaboration (Higgins & Green, 2005), when study outcomes were heterogeneous, a random (DerSimonian & Laird, 1986) rather than fixed model was applied to pool study data.

### ***III.iii Study description***

The 14 included studies had a total of 6286 participants but not all of these were included in the meta-analysis as some studies had several intervention groups that were not relevant (see Table III.II), leaving a total of 4743 participants (2473 in treatment and 2259 in control conditions) being included in this analysis. The content of the interventions is provided in Table III.II.

There were ten studies that looked at the effect of providing feedback from a single biomarker. In four studies (Audrain 1997, Burling 1991, Jamrozik 1984, Sanders 1989) feedback on carbon-monoxide was provided in a single session and compared with quit-smoking advice (see Table III.II). However, there were some differences in terms of

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<sup>11</sup> As events in this analysis (i.e. cessation) are desirable rather than undesirable, it would be preferable to use a more neutral term than risk (such as probability), but, for the sake of convention, the terms risk and risk difference will be used throughout

who delivered the intervention and where it was delivered. A nurse carried out the intervention in two studies (Burling 1991, Sanders 1989), while trained health educators delivered the intervention in one (Audrain 1997) and GPs in the other remaining study (Jamrozik 1984). Two studies (Jamrozik 1984, Sanders 1989) were set in primary care, one was set in a smokers' clinic (Audrain 1997) and one (Burling 1991) in an antenatal clinic.

Two studies evaluated the impact of giving nicotine metabolite feedback by means of a point-of-care test compared with a minimal intervention comprising quit advice, a leaflet and the point-of care test but with delayed feedback (Barnfather 2005, Cope 2003). Again, there were differences with regard to the study delivery and location. In one study (Barnfather 2005), the intervention took place in a general dental practice and was delivered by the dentists, whereas the other study (Cope 2003) was carried out in an antenatal clinic, although it is unclear who provided the intervention. The effect of providing feedback of carotid ultrasound scans (a print-out of a picture imaging the arterial walls together with a relevant explanation of its significance) was assessed in two studies and compared with standard quit advice (Bovet 2002, Shahab 2007). While one of these studies was carried out in a patient population attending a cardiovascular clinic (Shahab 2007) the other selected participants from the general population (Bovet 2002). In both cases, the intervention was provided by a clinician. Two studies (Audrain 1997, Ito 2006) evaluated the impact of providing genetic risk feedback. Though the exact biomarker differed (Ito 2006 provided feedback on L-myc polymorphism, Audrain 1997 on CYP2D6), both biomarkers are associated with an increase in cancer risk. However, in one study in addition to cancer risk feedback, carbon-monoxide feedback and quit advice was also provided (Audrain 1997), while in the other (Ito 2006) only genetic risk feedback was given.

Table III.II Study summary

Reference	Sample and setting	Study Objective	Biomarker	Outcome Assessment	Follow-up	Design	Main Findings
Audrain <i>et al.</i> (1997)	550 smokers in stop smoking clinic; USA	Evaluation of long-term impact of susceptibility biomarkers on smoking behaviour change & symptoms of depression	CO levels; genetic marker for lung cancer (CYP2D6)	Smoking cessation by self-report	12 months	RCT-3 groups: (i) quit-smoking counselling (QSC); (ii) QSC+CO feedback (EBF); (iii) QSC+EBF+cancer susceptibility feedback	Participants in (iii) twice as likely to make quit attempt but no group differences in cessation rates & depression scores
Barnfather <i>et al.</i> (2005)	97 smokers in Dental Practice; UK	To investigate the effect of immediate feedback from a point of care (POC) test for promoting cessation/reduction in tobacco use	Metabolic break down products of nicotine (e.g. cotinine levels)	Smoking cessation/reduction by POC test	8 weeks	RCT-2 groups: (i) quit smoking advice (including pictures of oral disease)+POC test (delayed feedback); (ii) as (i) with immediate POC feedback	Participants in (ii) sig. more likely to have quit/reduced tobacco consumption and have lower metabolite levels
Bovet <i>et al.</i> (2002)	155 smokers from general population; Seychelles	To examine whether visualisation - and thus increased awareness - of atherosclerosis improves smoking cessation	Ultrasound photograph of arteries	Smoking cessation by self-report	6 months	RCT-3 groups: (i) smoking cessation counselling; (iia) smoking cessation counselling+smoking cessation counselling+ultrasonography; (iib) same as (iia)+photo of own ultrasound	Participants in (iia+b) had sig. higher cessation rates than (i), highest cessation rates were found for participants in (iib)
Burling <i>et al.</i> (1991)	139 healthy pregnant smokers in antenatal clinic; USA	To assess the influence of minimal intervention (bio-markers and advice) on smoking cessation during pregnancy	Breath carbon monoxide (CO) levels	Smoking cessation by exhaled CO	4 & 10 weeks	RCT-2 groups: (i) usual care (including quit-smoking advice); (ii) same as (i) + personal letter including biomarker feedback	Cessation rate at 4 but not at 10 weeks was significantly higher for (ii) than (i)
Cope <i>et al.</i> (2003)	282 healthy pregnant smokers in antenatal clinic; UK	To investigate a point of care urine (POC) test for smoking & to relate test results to pregnancy outcome	Metabolic nicotine break down products (e.g. cotinine)	Smoking cessation/reduction by POC test	Approx 12 weeks	RCT-2 groups: (i) quit-smoking advice + POC test (delayed feed-back); (ii) POC test (immediate feedback)+ specific counselling (agreeing on quit date + leaflet)	Smoking test results within (ii) fell sig. from time 1 to 2, and were significantly lower than in (i) at time 2

Reference	Sample and setting	Study Objective	Biomarker	Outcome Assessment	Follow-up	Design	Main Findings
Ito <i>et al.</i> (2006)	697 smokers in cancer hospital clinic; Japan	To evaluate whether feedback of genetic information regarding cancer risk has an influence on smoking cessation	Genotype of <i>L-myc</i> polymorphism (no increased risk: LL; increased risk: LS/SS)	Smoking cessation by self-report	3 and 9 months	RCT-2 groups: (i) followed up to monitor cessation – no intervention, (ii) cancer susceptibility feedback	There were no sig. differences between groups at follow-up but risky phenotype feedback increased cessation in non-cancer patients
Jamrozik <i>et al.</i> (1984)	2110 smokers in general practice; UK	To investigate the efficacy of providing various anti-smoking interventions in primary care	Breath carbon monoxide (CO) levels	Smoking cessation/quit attempt by self-report / cotinine in sub-sample	12 months	RCT-4 groups: (i) control – no intervention; (ii) verbal & written antismoking advice; (iii) as (ii) + CO feedback; (iv) as (ii) + offer of further help from a health visitor	Significant increase of cessation rates in intervention groups compared with control group
Richmond <i>et al.</i> (1985)	200 smokers in general practice; Australia	To test the effectiveness of a GP based smoking intervention programme comprising biomarker feedback & counselling	Spirometry, carboxy-haemoglobin and thio-cyanate test	Smoking cessation by blood test	6 months	RCT-2 groups: (i) several counselling visits; (ii) six counselling visits including biomarker feedback	33% in (ii) vs. 3% in (i) had quit smoking; comparison shows quitters were sig. motivated by biomarker feedback
Risser <i>et al.</i> (1990)	90 smokers in general screening clinic; USA	To test whether adding information about personal effects of smoking would motivate outpatients more than advice to quit	CO levels, spirometry & pulmonary symptoms	Smoking cessation by exhaled CO	1, 4 and 12 months	RCT-2 groups: (i) counselling, quit advice+self-help manual+invitation to 9-session counselling programme;(ii) as (i) + biomarker feedback	Participants in (ii) more likely to have quit some time during the year but no sig. differences were confirmed by CO level
Sanders <i>et al.</i> (1989)	751 smokers in general practice; UK	To assess the effectiveness of anti-smoking advice provided by nurses	Breath carbon monoxide (CO) levels	Smoking cessation by self-report or cotinine in subsample	13 months	RCT-3 groups: (i) Control (no intervention); (ii) Health check +discussion of disease history in family+quit advice+booklet; (iii) as (ii) with CO feedback	Smoking in (ii) and (iii) sig. reduced at follow up compared with control but no difference among intervention groups (ii) and (iii)

Reference	Sample and setting	Study Objective	Biomarker	Outcome Assessment	Follow-up	Design	Main Findings
Segnan <i>et al.</i> (1991)	923 smokers in general practice; Italy	To examine the effectiveness of different practice-based approaches to assist patients in primary care to stop smoking	Spirometry	Smoking cessation by cotinine	6 & 12 months	RCT-4 groups: (i) Minimal singular intervention (advice+ brochure); (ii) as (i) but on four occasions; (iii) as (ii) with NRT; (iv) as (ii) with spirometry feedback	There were no significant differences between groups in terms of cessation
Shahab <i>et al.</i> (2007)	23 patients in cardiovascular clinic; UK	To examine the potential impact of visual, personalised biomarker feedback on smoking cessation behaviours	Ultrasound photograph of arteries	Smoking cessation behaviours by self-report	1 month	RCT-2 groups: (i) Smoking cessation advice+scan+routine feedback (ii) as (i) with visual scan feedback+leaflet	No differences between groups in terms of cessation but differences in various cessation behaviours
Sippel <i>et al.</i> (1999)	205 smokers in primary care clinic	To determine effectiveness of biomarker intervention in comparison with standard quit advice	CO levels & spirometry	Smoking cessation/quit attempt by self-report	6-9 months	RCT-2 groups: (i) standard quit smoking advice+written material; (ii) as (i) with CO and spirometry feedback	No difference in smoking cessation but tendency to make at least one quit attempt in (ii) compared with (i)
Walker <i>et al.</i> (1985)	64 smokers in stop smoking clinic; USA	To assess the effect of taste satiation (TS) and focused smoking (FS) treatments in combination with biomarker feedback	CO levels & spirometry	Smoking cessation by exhaled CO	1, 3 & 6 months	RCT 2-2-2 Factorial design: (i) TS (in 50%) or FS (in 50%) + booster session for half of each subgroup; as (ii) with CO and spirometry feedback	No difference between groups by biomarker feedback

### Chapter III: Systematic review – biomarkers in smoking interventions

Table III.III provides an overview of the study samples (N=14) and the level of sophistication of provided control and intervention conditions. Differences in the control conditions were minimal in the Ito study (simple follow-up to monitor session) and intensive in the Audrain study (same as treatment condition but no genetic risk feedback). Moreover, one study (Ito 2006) was carried out in a patient sample in an outpatient clinic (it is unclear by whom) and the other in a general population sample in a stop smoking clinic delivered by a health educator (Audrain 1997). Just one study (Segnan 1991) looked at the effect of spirometry testing alone (which determines lung function) on smoking cessation. The intervention, which was carried out by a physician in general practice, comprised a spirometry test (providing 'lung age') together with quit advice and written material. Quit advice was reinforced at a further three sessions. In the control condition, participants also received a brochure and repeated quit advice.

Three studies evaluated the combination of spirometry feedback with carbon-monoxide feedback. Two studies also included quit advice and written material in the intervention (Risser 1990, Sippel 1999) comparing it with a control condition comprising only quit advice and written material; the other study (Walker 1985) used a 2x2x2 factorial design whereby spirometry and CO feedback in the intervention condition was combined with either focused smoking, FS (no inhalation but focusing on unpleasant sensation of smoking) or taste satiation, TS (same as focused smoking but interspersed with inhalation of smoke into lungs) in half of the participants. Of these, a further half were randomised to receive TS or FS booster sessions. The same applied in the control group - half had TS and half FS and within each of the TS and FS groups, half had booster sessions. These interventions were delivered by a nurse in a general screening clinic in one (Risser 1990) and a study staff member in either a primary care or stop smoking clinic in the other two studies (Sippel 1999 and Walker 1985, respectively).



**Table III.III Participant and intervention characteristics of included studies**

Reference	Population Demographics				Intervention			
	Mean age (yrs)	Female (%)	White (%)	High School Education~ (%)	Mean Smoking (cig/day)	Length	Com-plexity <sup>#</sup>	Control Level*
Audrain <i>et al.</i> (1997)	44	63	84	84	22.5	1x80 min	high	high
Barnfather <i>et al.</i> (2005)	34	50	-	-	-	1 session	medium	medium
Bovet <i>et al.</i> (2002)	45	20	0	24	10-12	1x25 min	high	medium
Burling <i>et al.</i> (1991)	23	100	53	On average low	12.7	1 session	low	low
Cope <i>et al.</i> (2003)	-	100	-	-	11.8	Several meetings	high	low to medium
Ito <i>et al.</i> (2006)	46.5	40.5	-	-	22	5-10 min	medium	low
Jamrozik <i>et al.</i> (1984)	-	65	-	-	-	1 session	medium	medium
Richmond <i>et al.</i> (1985)	16-65	-	-	-	-	6 sessions	high	low
Risser <i>et al.</i> (1990)	56	4	-	>66	23.5	60 min	medium	medium
Sanders <i>et al.</i> (1989)	38.5	-	-	-	-	1 session	high	high
Segnan <i>et al.</i> (1991)	20-60	38	-	75	16.9 <sup>^</sup>	4 sessions	high	high
Shahab <i>et al.</i> (2007)	62.8	47.8	-	26.1	12.3 <sup>^</sup>	1 session	medium	medium
Sippel <i>et al.</i> (1999)	38.5	62.5	86	50	20	10-15 min	high	high
Walker <i>et al.</i> (1985)	35.5	59	-	-	29.2	5x45 min	high	high

~A-level or equivalent; <sup>#</sup>Complexity refers to number of materials used in the intervention, the more complex, the more materials used (e.g. pamphlets/visual aids etc); \*Level of sophistication of treatment in control group (N.B. in cases of more than two study groups, control group refers to group most closely matching biomarker intervention group) <sup>^</sup>Derived from categorical data

Through comparison with a control group not receiving any biomarker feedback, the Audrain study, already described above, also enabled an evaluation of effectiveness of combining CO with genetic risk feedback. One last study evaluated the combination of three biomarkers (blood carboxyhaemoglobin, thiocyanite and spirometry) together with anti-smoking counselling provided on several occasions (Richmond 1985). In the control condition, participants were not given any biomarker test or feedback and received counselling on two occasions. The intervention and control conditions were carried out by four doctors in general practice.

### **III.iv Study Quality Assessment**

Since this review aimed to evaluate the effectiveness of interventions incorporating biomarker feedback and both poor design of studies and lack of rigour in execution of a study may result in biased estimates of effects, this section will assess the methodological quality of the included studies (summarised in Table III.II and Table III.IV).

#### **III.iv.i Susceptibility to Bias**

As the total attrition rate of studies varied from 0 to 47%, it is likely that some of the reports may have been affected by attrition bias. However, inclusion of missing participant data in the analysis according to intention-to-treat can limit and protect against this distortion and is therefore absolutely essential to guarantee the integrity of results (Kazdin, 1992). It is surprising then that three studies (Burling 1991, Cope 2003 and Walker 1985) did not specify whether an intention to treat analysis was performed and that one study did not use intention to treat in statistical analysis (Barnfather 2005) despite a considerable or unknown attrition rate. While Audrain 1997 did not employ an intention-to-treat analysis either, an analysis of dropouts revealed no differences compared with the retained sample (see Table III.III and Table III.IV).

Selection bias, a systematic difference between participants included and excluded in studies, is protected against by appropriate sampling procedures and randomisation of participants to treatment conditions. As described in III.iii, the method of recruitment as well as the population sampled in included studies were rather heterogeneous (Table III.II and Table III.III). Six studies recruited in primary care (Barnfather 2005, Jamrozik 1984, Richmond 1985, Sanders 1989, Segnan 1991, Sippel 1999) but two studies (Jamrozik 1984, Segnan 1991) restrict sampling to specific days and only three

### Chapter III: Systematic review – biomarkers in smoking interventions

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(Barnfather 2005, Sanders 1989, Sippel 1999) did not restrict sampling while one study (Richmond 1985) did not specify recruitment procedures. Two studies (Burling 1991, Cope 2003) recruited from the total sample of healthy pregnant women attending antenatal clinics during the study period, and another two studies (Ito 2006, Shahab 2007) recruited from a sample of outpatients in the hospital setting of which one (Ito 2006) only included outpatients visiting for the first time while the other (Shahab 2007) had no restrictions.

Two studies conducted in smoking cessation clinics recruited from the general population via media advertisement (Audrain 1997, Walker 1985), one study (Bovet 2002) recruited from the general population consecutive smokers who participated in a health survey and the remaining study (Risser 1990) from a sample of veterans who had agreed to attend a health screening programme. Unfortunately, most studies did not report participation rate (i.e. the proportion of people approached who agreed to take part) thus making it impossible to assess the degree of representativeness of the included sample.

Although only RCT studies were included in this review, just four studies used adequate randomisation procedures (Barnfather 2005, Risser 1990, Segnan 1991, Shahab 2007; see Table III.IV, footnote 12). Six studies reported using substandard randomisation procedures allocating participants on the day or week of attendance (Ito 2006, Jamrozik 1984, Sanders 1989), on the basis of alternation (even/odd) or case records (Cope 2003, Richmond 1985, Sippel 1999), and four studies (Audrain 1997, Bovet 2002, Burling 1991, Walker 1985) did not specify how the randomisation was carried out.

Table III.IV Methodological quality of included studies (N=14)

Reference	True Randomisation <sup>12</sup>	Matching of Group Characteristics	Matching of Treatment	Standardisation of Procedures	Trained Staff	Validation of Measures	Blinding of Assessor	Total Attrition	Intention to treat Analysis	Appropriate Statistic
Audrain <i>et al.</i> (1997)	Not specified	Yes, on extensive baseline measures, no differences	Yes	Yes	Yes	Partly	Not known	23 %	Not known	Unclear: $\chi^2$ , ANOVA, logistic regression
Barnfather <i>et al.</i> (2005)	Yes	Yes, on minimal baseline measures no differences	Yes	Yes	No	Yes	Not known	10.3%	No	Yes: $\chi^2$ ; Mann-Whitney U
Bovet <i>et al.</i> (2002)	Not specified	Yes, on minimal baseline measures, no differences	Yes	Not known	No	Not known	Yes	1%	No	Unclear: Fisher's Exact Test, ANOVA, logistic regression
Burling <i>et al.</i> (1991)	Not specified	Not known	Yes	Yes	Yes	Yes	Not known	Not known	Not known	Unclear: t-test, ANOVA
Cope <i>et al.</i> (2003)	No, on basis of hospital number	Not known	No	Not known	Yes	Yes	Not known	31 %	Not known	Unclear: Wilcoxon, ANOVA

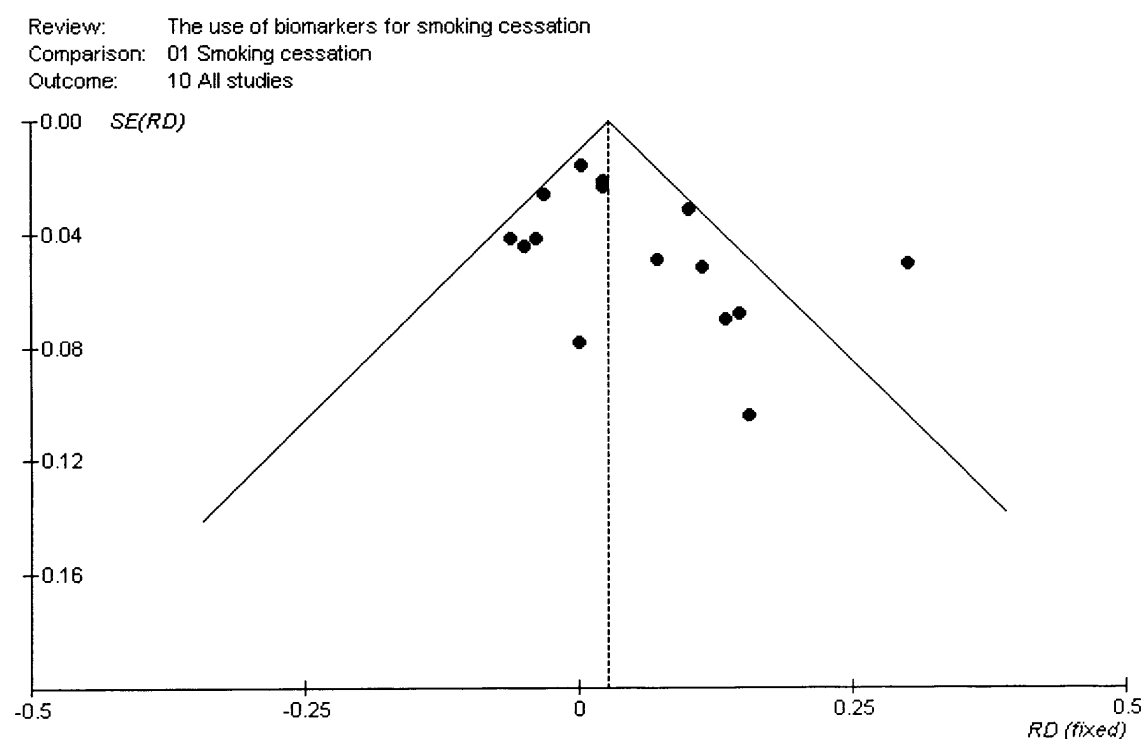
<sup>12</sup> The use of alternation, case record numbers, birth dates or week days is considered to be inadequate for randomisation (Verhagen, de Vet, de Bie, Kessels *et al.*, 1998)

Reference	True Randomisation <sup>12</sup>	Matching of Group Characteristics	Matching of Treatment	Standardisation of Procedures	Trained Staff	Validation of Measures	Blinding of Assessor	Total Attrition	Intention to treat Analysis	Appropriate Statistic
Ito <i>et al.</i> (2006)	No, on basis of week of attendance	No; on extensive baseline measures, sig. higher alcohol consumption in control group	No	Not known	Yes	Partly	Not known	47%	Yes	Yes: $\chi^2$ , Wilcoxon, logistic regression
Jamrozik <i>et al.</i> (1984)	No, on basis of day of attendance	No, people in intervention on average in higher socioeconomic group	Yes	Yes	Yes	Yes	No	28%	Yes	Statistics not provided
Richmond <i>et al.</i> (1985)	No, on basis of alternation	Not known	No	Yes	No	Yes	Not known	24%	Yes	Yes: $\chi^2$
Risser <i>et al.</i> (1990)	Yes	Yes, on extensive baseline measures, no differences	Yes	Yes	Yes	Yes	Yes	21%	Yes	No: $\chi^2$
Sanders <i>et al.</i> (1989)	No, on basis of day of attendance	Not known	Yes	Yes	Yes	Yes	No	36.2%	Yes	Unclear: t-test, $\chi^2$

Reference	True Randomisation <sup>12</sup>	Matching of Group Characteristics	Matching of Treatment	Standardisation of Procedures	Trained Staff	Validation of Measures	Blinding of Assessor	Total Attrition	Intention to treat Analysis	Appropriate Statistic
Segnan <i>et al.</i> (1991)	Yes	Yes	Yes	Yes	Yes	Yes	Not known	23%	Yes	Statistics not provided
Shahab <i>et al.</i> (2007)	Yes	Yes	Yes	Yes	Yes	Partly	Not known	0%	N/A	Yes: $\chi^2$ ; Mann-Whitney U, Fisher's Exact Test, ANOVA
Sippel <i>et al.</i> (1999)	No, on basis of alternation	Yes	Yes	Yes	Yes	Partly	Yes	15.6%	Yes	Unclear: $\chi^2$ ; t-test; logistic regression
Walker <i>et al.</i> (1985)	Not specified	Yes	Yes	Yes	Yes	Yes	Not known	6.25%	Unclear	No: $\chi^2$ , ANOVA

Publication bias or “file drawer” problem, i.e. the fact that non-significant results are less likely to be published or submitted for publication, has long been acknowledged as a potential issue for meta-analyses (e.g. Begg & Berlin, 1989). One way to determine whether publication bias is likely to affect meta-analyses is by means of funnel plots, where the treatment effect is plotted against some measure of the study sample size, e.g. the standard error of the effect estimate (Egger, Davey Smith G., Schneider, & Minder, 1997). As precision of the estimate of the true treatment effect increases with the study sample size, small studies scatter at the bottom (the wide part of the funnel), and the spread narrows among larger studies. When no bias exists, the spread should resemble an inverted funnel, but in the presence of publication bias, asymmetry is observed (e.g. Berlin, Begg, & Louis, 1989). Figure III.I provides a funnel plot for the studies included in this review.

**Figure III.I: Funnel plot of included studies**



It appears that results are relatively symmetrically spread around the mean effect estimate, with one positive outlier. However, there is some suggestion of publication bias with regards to small studies finding negative effects, which would appear in the lower left quadrant of the plot. This implies that the effect calculated from all studies may overestimate the treatment effect (Villar, Piaggio, Carroli, & Donner, 1997), and for this reason no such overall treatment effect will be presented.

Lastly, in order to reduce measurement or detection bias, the blinding of outcome assessors to participants treatment allocation is also crucial (Schulz, Chalmers *et al.*, 1995). However, of the selected studies, only three studies (Bovet 2002, Risser 1990, Sippel 1999) explicitly stated that assessors were blinded when the outcome was assessed, and in the majority of studies the status of blinding was unknown (Table III.IV).

#### **III.iv.ii Matching**

For the purpose of reducing the influence of confounding variables and to increase what can be meaningfully said about the study outcome, it is important to start with matched or equivalent comparison groups (Meltzoff, 1998). Similarly, the conditions of the treatment and control group should be matched as this will eliminate performance bias, i.e. systematic differences in the care provided, apart from the intervention being evaluated (Khan, ter Riet, Popay, Nixon *et al.*, 2001). In this cohort of studies, nine papers commented on the similarity of group characteristics (see Table III.IV), two of which (Ito 2006, Jamrozik 1984) unmasked significant differences between the intervention and control group, which were taken into consideration for analysis only in the Jamrozik study. It is also surprising to note the lack of sufficient information on basic socio-demographic and smoking characteristics for many of the study samples (see Table III.III), which – especially in studies not using correct randomisation



procedures - precludes an assessment of the equivalence in terms of these (potentially confounding) characteristics in control and intervention groups.

Regarding the matching of treatment and control group content, although the majority of studies attempted to minimise the differences between control and intervention conditions, three studies (Cope 2003, Ito 2006, Richmond 1985) did not take particular care to eradicate these differences (see Table III.II through Table III.IV). This imbalance between control and intervention introduces a number of problems as it becomes harder to evaluate whether changes between both groups were due to the intervention or other, spurious, variables. Lack of matching, for instance, can lead to a Hawthorne effect (Mayo, 1933), where people show different response rates because of the increased attention afforded in the intervention compared with the control group, not because of the actual intervention itself. However, it should also be noted that most studies (eleven out of fourteen) employed standardised procedures throughout the study as well as using trained staff, which is seen to reduce the possible effects of insufficient treatment matching (Khan, ter Riet *et al.*, 2001).

### **III.iv.iii Measurement of Constructs**

Most studies used well-validated questionnaires and other measurement tools to validate constructs that were assessed. However, two studies did not report whether some of their questionnaire items were validated (Bovet 2002, Ito 2006). Bovet *et al.* (2002) used a structured questionnaire to assess participants' knowledge, attitudes and practices on smoking and health without either identifying it or providing information about its reliability or validity. Ito *et al.* (2006) employed a survey, which evaluated risk perceptions of smoking-related diseases, level of fear arousal as well as readiness to quit smoking but did not provide any details on previous validation of these items. The lack of appropriate validation of construct measures is of concern for evaluating the

generalisability of study findings, since measures which have not been tested in other circumstances may be susceptible to various biases and unpredictable factors. This could lead to results becoming skewed.

With regard to the validation of outcomes, in particular smoking cessation, only half of the studies used an objective marker to assess smoking status (see Table III.II). Two studies (Jamrozik 1984, Sanders 1989) objectively verified smoking status only in a sub-sample and discovered high rates of misreporting (around 25%) whereas the remaining five studies (Audrain 1997, Bovet 2002, Ito 2006, Shahab 2007, Sippel 1999) just used self-report to assess smoking status. This, taken together with inconsistencies in the definition of abstinence between studies (as either point prevalence or continuous abstinence) is likely to make results both more heterogeneous and, in the case of self-report, less reliable.

### **III.iv.iv Statistical analysis**

Only one study used power calculation to formally estimate the required sample size before recruitment (Sippel 1999) but was overly optimistic in the estimate. Assuming a realistic difference between groups in terms of cessation of around 2-5%, i.e. a small effect (Cohen's  $w=0.1$ ), this would require a sample of at least 393 participants per group to establish this difference statistically at a significance level of 5% and with a power of 80%. Of the included studies only one (Jamrozik 1984) reached this number of participants, and several studies (Barnfather 2005, Bovet 2002, Risser 1990, Shahab 2007, Walker 1985) were severely underpowered ( $N<50$  per group) to detect anything other than very large effects leaving open the possibility of Type II error in their analyses.

Especially older studies provided little, if any, information on the statistical analyses used. The majority of studies used chi-square ( $\chi^2$ ) analysis or multivariate logistic regression to determine the impact of intervention on smoking cessation, while some also used ANOVA or t-tests to evaluate continuous outcomes (see Table III.IV). However, a number of studies did not report testing for parametric assumptions despite using parametric tests (Audrain 1997, Bovet 2002, Burling 1991, Cope 2003, Sanders 1989, Sippel 1999). Thus, when using t-tests or ANOVAs to examine differences between the intervention and control group on continuous variables, no care was taken to assess the influence of outliers on the result. For a more reliable result, these studies should have specifically tested for the assumptions of normal distribution and homogeneity of variance and/or used equivalent non-parametric tests (e.g. Mann-Whitney U or Kruskal Wallis) to determine the stability of results.

Moreover, two studies appear to have used incorrect statistical techniques to evaluate results. Risser *et al.* (1990) employed chi-square analysis to test the association between group allocation and smoking cessation. However, one of the requirements for chi-square analysis is that expected cell frequencies are 5 or above as expected frequencies below 5 violate the normality assumption (Overall, 1980), and in this study at least one of the expected cell frequencies fell below 5. This would make Fisher's Exact Probability test somewhat preferable, not only because it does not require this assumption, but also because it is more robust when analysing a 2x2 contingency tables (Howell, 1997). Walker *et al.* (1985) assessed differences in proportions in a 2x2x2 factorial design with an ANOVA when in fact a logit model or chi-square tests would have been appropriate considering that the outcome (smoking cessation) was not continuous. Finally, as was mentioned before, not only did many of the studies show an appreciable attrition rate, but in some studies there also existed some group differences

at baseline. It would therefore have been preferable to use statistical methods that can adjust for confounding (such as logistic regression), yet only very few had measured possible confounders (especially smoking characteristics) and adjusted for these (Audrain 1997, Bovet 2002, Ito 2006). For instance, one study (Sippel 1999) did not adjust for a serious confounding variable (NRT use) when evaluating the impact of the intervention on cessation.

Altogether, considering the above caveats regarding methodology, the quality of included studies can best be described as moderate to low.

### **III.v Results**

#### **III.v.i Smoking Cessation**

A total of five studies (Barnfather 2005., Bovet 2002, Cope 2003, Richmond 1985, Risser 1990) reported a significant or near significant impact of biomarker feedback on smoking cessation. An additional three studies reported significant results at either an earlier follow-up point (Burling 1991) or in comparison of biomarker feedback with minimal control groups that had received no input other than being followed up to determine smoking status (Jamrozik 1984, Sanders 1989). Owing to the disparity in study design both in terms of the length of follow-up and the biomarker feedback included, results were analysed separately according to these criteria and not pooled.

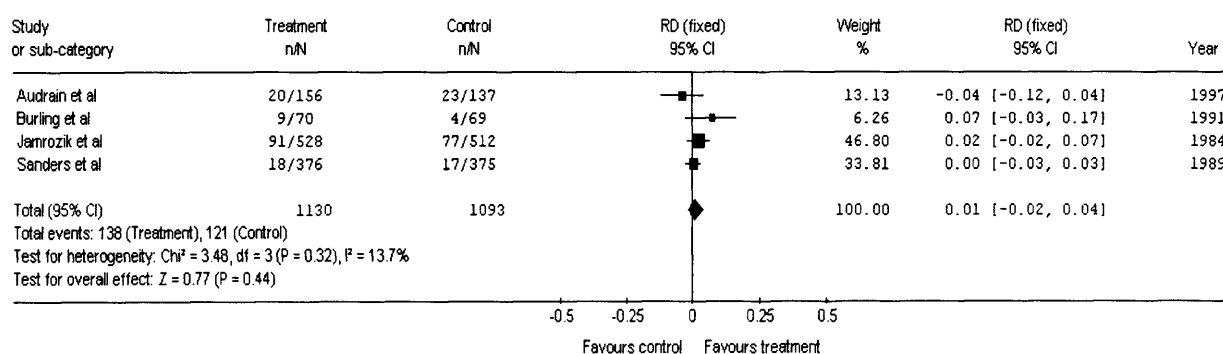
##### **III.v.i.i Smoking cessation and feedback from a single biomarker**

As described in III.iii, while all papers reviewed provided biomarker feedback, they did not all employ the same biomarker (see also Table III.II). When evaluating the outcome results by the biomarker used, it becomes evident that there is no singular consistent association between biomarker feedback and cessation. Indeed, when looking only at the studies that used one biomarker rather than a combination of these, results are significantly non-homogeneous ( $I^2=55.2\%$ ;  $\chi^2(10)=22.6$ ,  $p=0.01$ ). Assessing the overall

impact of providing feedback from a single biomarker suggests that while there as in increase in cessation rates of 2% associated with feedback, this difference is not significantly different from the control conditions ( $Z=1.62$ ,  $p=0.11$ ). As can be seen from looking at the pooled results of studies that have used the same biomarker to provide feedback, outcomes were somewhat contradictory.

## Figure III.II: CO feedback<sup>#</sup>

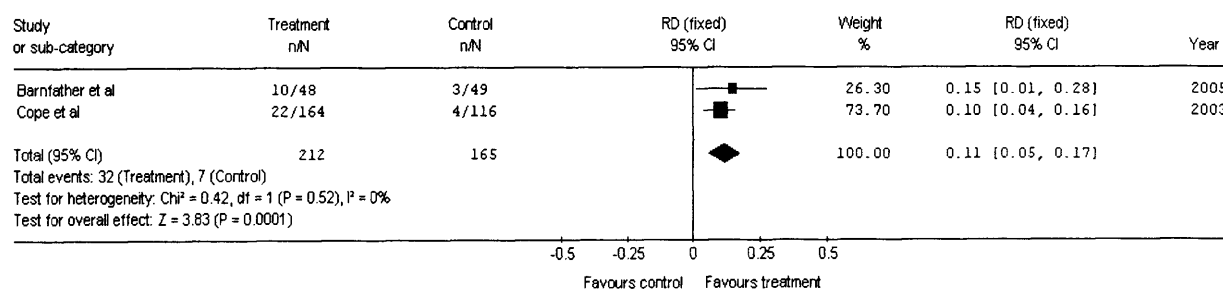
Review: The use of biomarkers for smoking cessation  
Comparison: 01 Smoking cessation  
Outcome: 05 CO feedback



<sup>#</sup>RD – Risk difference; Audrain 1997 provided three comparison (CO feedback, genetic feedback and combination of CO and genetic feedback)

## Figure III.III: Nicotine metabolite feedback<sup>#</sup>

Review: The use of biomarkers for smoking cessation  
Comparison: 01 Smoking cessation  
Outcome: 06 Nicotine metabolite feedback



<sup>#</sup>RD – Risk difference

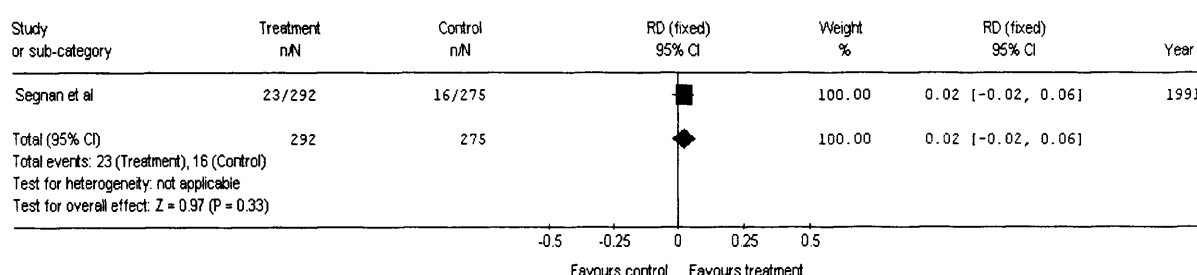
Thus among exposure biomarkers, studies looking at CO feedback on the whole found no significant impact on cessation (see Figure III.II)<sup>13</sup>, whereas the studies using nicotine metabolite feedback did (see Figure III.III) despite the disparity in settings (general practice in Barnfather study and antenatal clinic in Cope study). The same is true when evaluating the impact of harm biomarker feedback. The study that used

<sup>13</sup> However, both Jamrozik and Sanders found a significant difference when comparing the intervention with a minimal rather than high intensity control group ( $p<0.05$  and  $p<0.01$ , respectively) and Burling reported a near significant result ( $p<0.1$ )

spirometry feedback (to show evidence of smoking-related harm to the lungs) did not find a significant effect on smoking cessation (see Figure III.IV), whereas the pooled result from studies that provided carotid ultrasound scan as evidence of smoking-related damage to the cardiovascular system suggests a ten percent increase (95%CI<sup>14</sup> 1-19%) in cessation rates (see Figure III.V).

## Figure III.IV: Spirometry feedback<sup>#</sup>

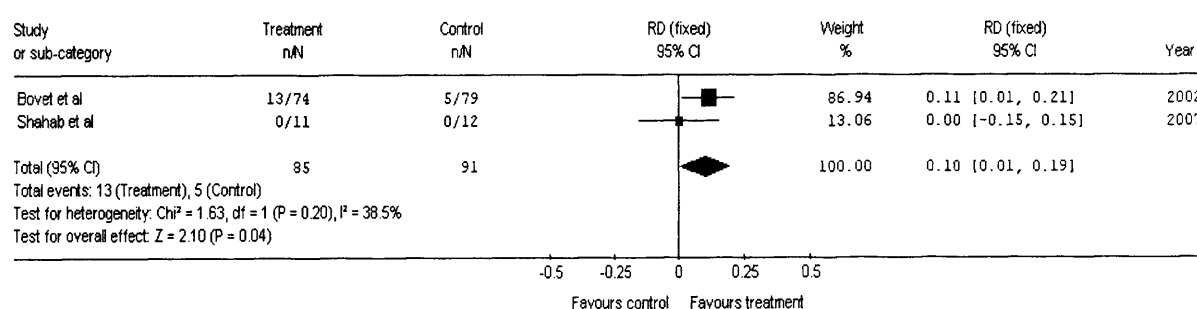
Review: The use of biomarkers for smoking cessation  
Comparison: 01 Smoking cessation  
Outcome: 09 Spirometry



<sup>#</sup>RD – Risk difference

## Figure III.V: Carotid ultrasound feedback<sup>#</sup>

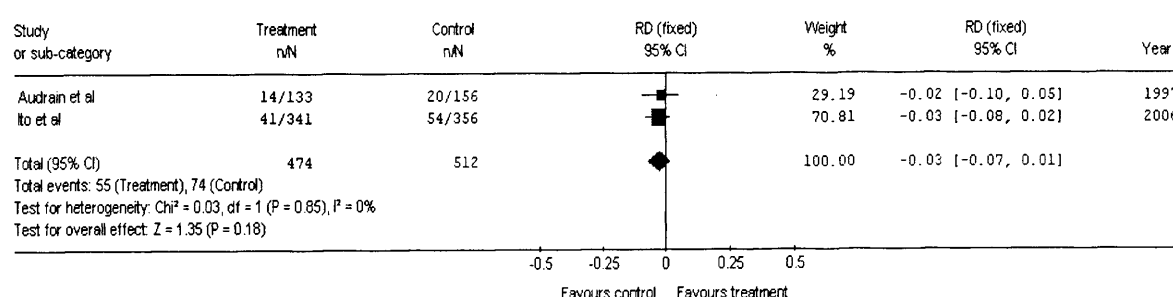
Review: The use of biomarkers for smoking cessation  
Comparison: 01 Smoking cessation  
Outcome: 08 Carotid US feedback



<sup>#</sup>RD – Risk difference

## Figure III.VI: Genetic risk feedback<sup>#</sup>

Review: The use of biomarkers for smoking cessation  
Comparison: 01 Smoking cessation  
Outcome: 07 Genetic risk feedback



<sup>14</sup> This stands for the 95% confidence interval for the measure under consideration, in this case the percent increase

## Chapter III: Systematic review – biomarkers in smoking interventions

#RD – Risk difference; Audrain 1997 provided three comparison (CO feedback, genetic feedback and combination of CO and genetic feedback)

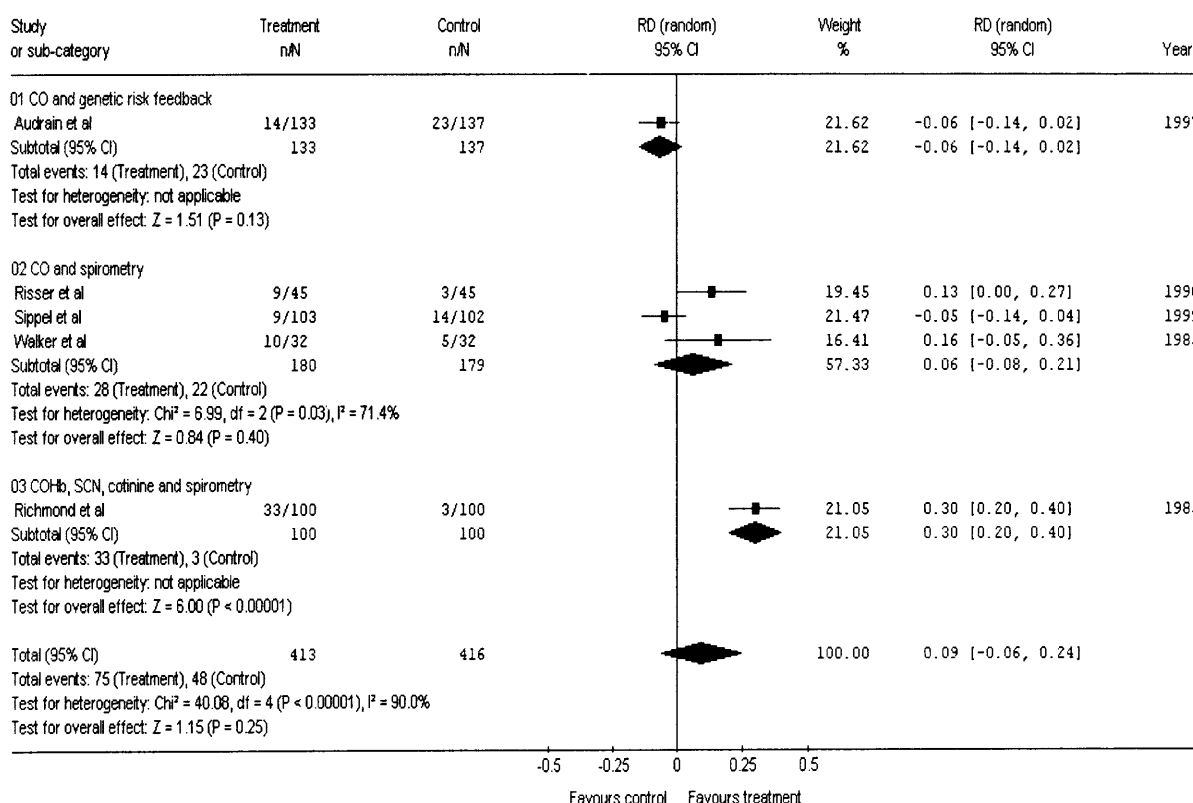
The only consistent finding in terms of the type of biomarker used is that provision of genetic risk biomarkers was not found to have a significant impact on smoking cessation and rather was associated with a decrease in quit rates in both studies that assessed this biomarker despite their considerable disparity in design (Figure III.VI).

### III.v.i.ii Smoking cessation and multiple biomarker feedback

A number of included studies looked at the combination of various biomarkers (see Table III.II).

**Figure III.VII: Biomarker combination<sup>#</sup>**

Review: The use of biomarkers for smoking cessation  
Comparison: 01 Smoking cessation  
Outcome: 02 Combination of biomarkers



#RD – Risk difference; Audrain 1997 provided three comparison (CO feedback, genetic feedback and combination of CO and genetic feedback); COHb (carboxyhaemoglobin), SCN (thiocyanate)

The amount of different biomarkers that were included in various interventions did not appear to relate to successful cessation. Thus studies comprising only one biomarker (e.g. Bovet 2002 or Cope 2003) produced similar effects to studies with two (e.g. Risser 1990) or three (Richmond 1985) biomarkers. As can be seen in Figure III.VII, there was

considerable heterogeneity in study results ( $I^2=90\%$ ;  $\chi^2(4)=40.08$ ,  $p<0.001$ ) and pooling suggested that while there is a 9% increase associated with receiving feedback from several biomarkers, this increase is not significant in a random effects model ( $Z=1.15$ ,  $p=0.25$ ).

However, when excluding studies with only very brief follow-up periods, the results of studies with at least a 6 month follow-up show that out of three significant or near significant results, two come from studies that provided several biomarkers (Richmond 1985, Risser 1990; see Figure III.IX). Moreover, as shown in Figure III.VII, the one study that produced the most impressive results (Richmond 1985) was also the study with most biomarkers included, suggesting that combining more biomarkers may prove beneficial for smoking cessation.

#### **III.v.i.iii Smoking cessation and biomarker feedback by length of follow-up**

A few papers (Burling 1991, Risser 1990, Segnan 1991, Walker 1985)<sup>15</sup> assessed smoking cessation several times during the course of the study. As would be expected, the effect of the intervention wears off at later follow-ups within these studies. Out of the four studies with two or more follow-ups, only one (Risser 1990) reported a slight increase in cessation rates as time progressed, whereas the remaining three studies reported a fall in smoking cessation from the first to the last measurement.

The same observation can be made when smoking cessation results are compared across studies with different follow-up times. When looking at smoking cessation rates assessed at less than six months, quit rates are significantly increased by 7% (95%CI 4-20%; see Figure III.VIII).

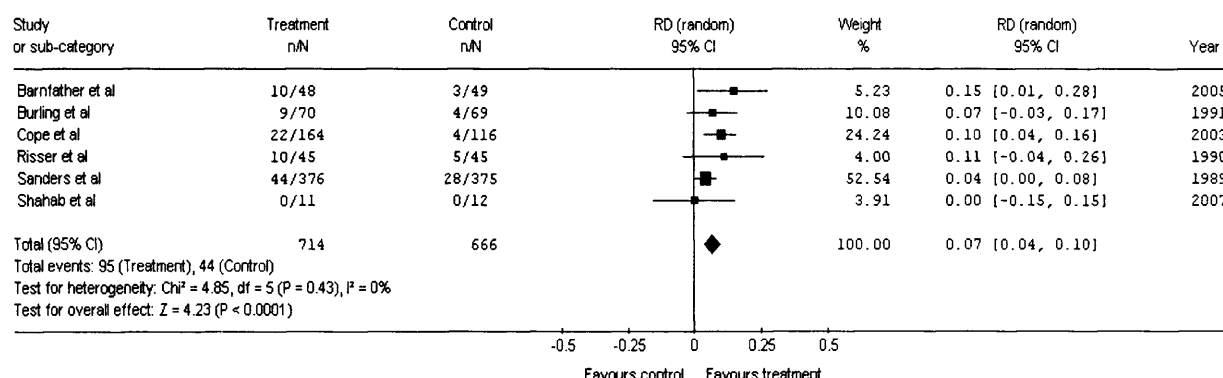
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<sup>15</sup> In the Ito 2006 paper, there is no separate analysis of the smoking cessation rates at different times despite several follow-ups



**Figure III.VIII: Studies with follow up below 6 months<sup>#</sup>**

Review: The use of biomarkers for smoking cessation  
 Comparison: 01 Smoking cessation  
 Outcome: 03 Follow-up < 6 months

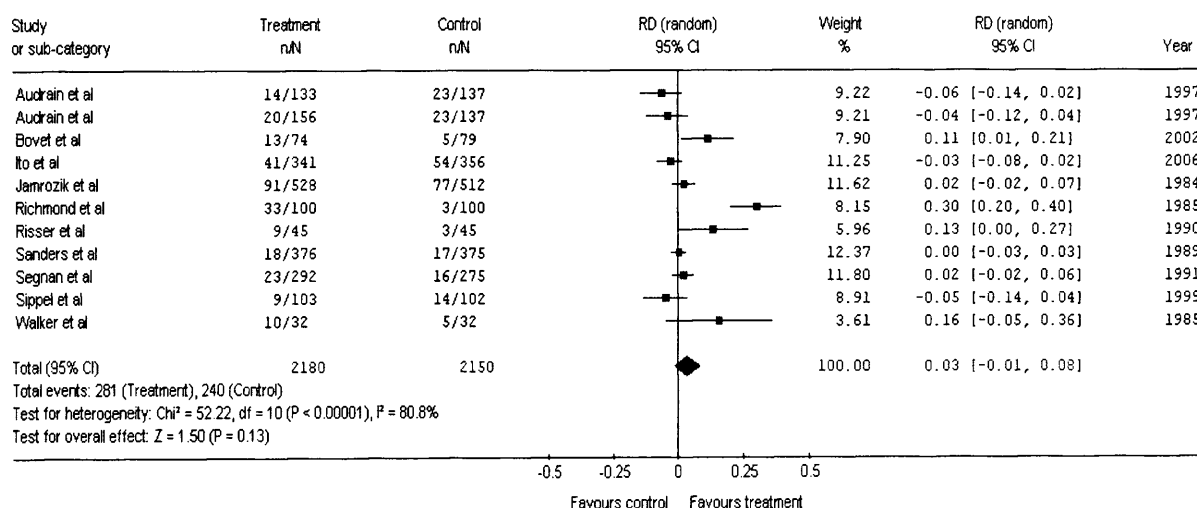


<sup>#</sup>RD – Risk difference

However, this quit rate is more than halved to 3% when the follow-up was carried out at least six months after the intervention, and this difference is not significant ( $Z=1.5$ ,  $p=0.13$ , see Figure III.IX)<sup>16</sup>.

**Figure III.IX: Studies with follow up at 6 months or more<sup>#</sup>**

Review: The use of biomarkers for smoking cessation  
 Comparison: 01 Smoking cessation  
 Outcome: 04 Follow-up  $\geq 6$  months



<sup>#</sup>RD – Risk difference

### III.v.i.iv Smoking cessation and intervention design

Despite the fact that smoking cessation was achieved at some point of measurement in a number of studies, it appears that findings of continuing abstinence are not as unanimous, and this may be related to the intervention designs that have been employed

<sup>16</sup> It should also be noted that outcomes across studies were very heterogeneous

in the various papers. Table III.III (see page 72) presents some of the main differences between the studies under review and includes a stratification of the level of sophistication of the diverging interventions and control conditions.

Of the two studies reporting a significant reduction in continuous abstinence at less than 6 months, one (Cope 2003) used a relatively complex intervention involving several counselling sessions but had a very poorly matched control group. Similarly, among the three studies that reported significant increases in continuous abstinence at six months or more, two (Bovet 2002 and Richmond 1985) had rather complex interventions, while the control condition included a bare minimum of counselling and quit advice. This relationship of complexity with outcome is further corroborated when considering studies with several control conditions. In both the Jamrozik and Sanders study no significant difference could be detected when comparing the intervention with a suitably complex control condition, but there was a significant effect of the intervention when comparing it with a simple control condition.

While both complexity and intensity of the intervention tend to be linked to successful cessation, neither seem necessary to produce this outcome. The relatively simple manipulation of presenting participants with a point-of-care urine test (Barnfather 2005) was as effective as more complex interventions using the same biomarker (Cope 2003). However, the former study did not have a very long follow-up period, which may have contributed to this effect. Another interesting finding relates to cigarette consumption and its association with outcome. It is noteworthy that of the ten studies that provided information on smoking characteristics, two studies with participants who were relatively light smokers (<15 cig/day) found a significant increase in cessation rates (Bovet 2002, Cope 2003) but of the studies with participants that had a high cigarette

consumption (>20 cig/day), just one reported a near significant increase in cessation (Risser 1990). In general it appears, the higher the level of sophistication of the control condition, the longer the follow-up and the higher the nicotine intake, the lesser the impact of the intervention on smoking cessation.

### **III.v.ii Other smoking-related outcomes**

Table III.V summarises other smoking-related outcomes assessed in included studies. Although not all studies found a significant impact of the intervention on cessation, the majority of studies achieved an improvement in at least one smoking-related outcome.

#### **III.v.ii.i Smoking reduction and quit attempts**

Smoking reduction was explicitly measured by five studies (Audrain 1997., Barnfather 2005, Bovet 2002, Burling 1991, Cope 2003) and one study measured a collection of smoking behaviours including smoking reduction (Shahab 2007). Of these, one study (Cope 2003) found a significant reduction in smoking, both within the intervention group, from the first to the last assessment approximately 3 months later, and between the intervention and control group, while another (Barnfather 2005) detected a significant reduction in smoke intake among cases compared with the control group. Although these findings were not confirmed by the other three studies, they cannot be easily dismissed as two studies found a near significant effect (Bovet 2002, Shahab 2007), and in none of the three studies was smoking reduction assessed with an objective measure. In contrast, both in the Barnfather and Cope study smoking reduction was verified by means of a nicotine metabolite.

Several studies (Audrain 1997, Jamrozik 1984, Risser 1990, Shahab 2007, Sippel 1999) included a measure of quit-attempts in their analysis, of which only one (Jamrozik 1984) found an outright non-significant result, while two reported a near-significant impact of the intervention (Shahab 2007, Sippel 1999), and two studies (Audrain 1997,

Risser 1990) detected that significantly more participants in the intervention than in the control condition had tried to stop smoking. This finding is further corroborated when one considers the Burling study, which reported a significant increase in smoking cessation rates at the earlier but not at the later assessment stage. Here, participants had attempted to quit smoking but were not able to maintain cessation for the whole study period, thereby implicitly confirming the observed impact on quit attempts.

### III.v.ii.i Moderating variables

A variety of moderating variables - shown in Table III.V - were assessed across papers. Of those included, neither self-efficacy nor risk perception appear to have moderated cessation. As reported in Audrain *et al.* (1997) there was also no association between depression and biomarker feedback; however, one study (Ito 2006) found that biomarker feedback increased fear levels, and another study reported an increase in perceived susceptibility to disease (Shahab 2007). This change in fear/susceptibility perceptions possibly explains the finding reported in two studies (Bovet 2002, Ito 2006) that only negative biomarker feedback (i.e. feedback that shows signs of disease or increased risk) was associated with increased quit rates, as in this case fear levels would be raised thus leading to behavioural modification. However, in one study (Sippel 1999) no impact of abnormal results on cessation rates was found.

In terms of other antecedents of behaviour change, intention or readiness to stop smoking<sup>17</sup> yielded incongruent effects. Audrain *et al.* (1997) reported that it moderated quit attempts - irrespective of treatment allocation - whereas the number of quit attempts was not affected by intention to quit in the analysis in Risser *et al.* (1990). Moreover, while self-efficacy had not impact on cessation rates in Audrain's study, it did interact with the intervention on intention to stop smoking in another study (Shahab 2007).

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<sup>17</sup> Measured by stages of change in Audrain 1997

**Table III.V Summary of secondary study results**

Reference	Smoking Reduction <sup>#</sup>	Quit Attempts <sup>#</sup>	Impact of moderating variables on intervention outcomes
Audrain <i>et al.</i> (1997)	Not significant	p = 0.05	<i>Cessation</i> : No impact of self-efficacy or stage of change; <i>Quit attempts</i> : Stages of change main effect (p<0.0001); <i>Depression</i> : no intervention impact
Barnfather <i>et al.</i> (2005)	p <0.001	-	-
Bovet <i>et al.</i> (2002)	p<0.07	-	<i>Cessation</i> : White collar job (OR=3.46) but no other demographics; impact in intervention only among those with plaque
Burling <i>et al.</i> (1991)	Not significant	-	<i>Cessation</i> : Time of intervention during earlier stages of gestation, p = 0.02
Cope <i>et al.</i> (2003)	In intervention & between groups (p<0.001&p=0.003)	-	-
Ito <i>et al.</i> (2006)	-	-	<i>Cessation</i> : Benefit for non-cancer patients who are women (OR= 3.6)/have risky genotype (OR =2.9); opposite for men with cancer (OR=0.4) <i>Fear</i> : Sig. increased by intervention (p<0.01)
Jamrozik <i>et al.</i> (1984)	-	Not significant	<i>Cessation</i> : Non-manual social class more likely to benefit from intervention but benefit of CO feedback in manual group
Richmond <i>et al.</i> (1985)	-	-	-
Risser <i>et al.</i> (1990)	-	p = 0.026	<i>Quit attempts</i> : Intention to quit had no impact; but quitters more motivated than non-quitters by spirometry (p=0.01) blood test feedback (p=0.02)
Sanders <i>et al.</i> (1989)	-	-	-
Segnan <i>et al.</i> (1991)	-	-	-
Shahab <i>et al.</i> (2007)	p<0.1	-	<i>Intention to quit</i> : Significant interaction by self-efficacy level (p=0.03); <i>Susceptibility</i> : Sig. increased by intervention (p=0.05)
Sippel <i>et al.</i> (1999)	-	p=0.09	<i>Cessation</i> : No impact of abnormal spirometry test but NRT use had (OR 6.7)
Walker <i>et al.</i> (1985)	-	-	<i>Cessation</i> : Biomarker feedback increased cessation in the focused smoking not the taste satiation group at 1 month follow up (p<0.05)

<sup>#</sup>In comparison with control

These disparities may be due to differences in construct measurement; Risser *et al.* (1990) recorded quit intentions orally, in Audrain's study quit intentions were assessed in written form and both Risser *et al.* (1990) and Shahab *et al.* (2007) used a different

measure than Audrain *et al.* (1997) to determine quit intentions. Moreover, these findings may arise from the different populations sampled; Audrain's sample was much larger, younger and more educated than either Risser or Shahab's sample, which may have confounded results. Indeed, one of the only demographic measures found to affect outcome was education. Bovet *et al.* (2002) reported that people with lower professional attainment were significantly more likely to quit smoking after the intervention. Lastly, it appears that having a disease was not associated with a greater likelihood of stopping smoking when receiving biomarker feedback - as shown by two studies involving patient samples (Ito 2006, Shahab 2007) - while receiving feedback early on in pregnancy increased the impact of the intervention (Burling 1991, see Table III.V).

#### **III.vi Discussion**

How do the findings of this review relate to the initial questions posed by the background literature? All of the studies included found evidence that biological feedback was significantly or near-significantly associated with either smoke reduction and/or increased attempts to quit and remain abstinent. This suggests that motivation to quit was improved across all studies as, indeed, was found in the studies that explicitly measured quit intentions. However, significant continuous abstinence could not be sustained in the majority of trials. This lack of significant smoking cessation across studies should, however, be weighed against the level of control – most unsuccessful interventions were compared with very sophisticated control conditions. The discrepancy between motivating people to quit smoking and the actual ability to turn this into something sustainable is not new. This 'motivation-behaviour gap' (Armitage & Conner, 2001) has a long history of documentation showing attitude-behaviour correlations as low as 0.3 (Wicker & Pomazal, 1971), which is confirmed by the contradictory results between intentions and behaviour reported for instance in Risser *et al.* (1990) and Audrain *et al.* (1997).

The effectiveness of interventions varied depending on the length of follow-up, control condition complexity and nicotine intake. This result is in keeping with research evidence demonstrating that after an initial high, abstinence rates fall over the length of smoking cessation treatments (e.g. Hunt, Barnett, & Branch, 1971). The impact of nicotine dependence and cigarette consumption on intervention outcomes has also been corroborated by numerous studies, which have shown that the number of cigarettes smoked per day relates inversely to cessation (e.g. Cohen, Lichtenstein, Prochaska, Rossi *et al.*, 1989).

What about the impact of different types of biomarkers? Early consensus was that the effectiveness of exposure biomarker feedback on its own as a tool to motivate cessation is unproven (e.g. Vogt, Selvin, & Hulley, 1979; Stitzer & Bigelow, 1982). In the light of the current findings, however, it appears that exposure biomarkers may have some utility. While CO feedback did not fare as well when compared with intensive control conditions, it did increase cessation rates compared with minimal control. Moreover, feedback of cotinine levels was associated with smoking cessation in the two studies that looked at the efficacy of a point-of-care test. Yet, some caveats need to be acknowledged. First, the observed effect of exposure biomarker feedback was commonly detected in pregnant women<sup>18</sup> and it could be speculated that these women may have been more motivated to quit smoking in order to avoid harming their unborn child (rather than themselves). The one study, which provided positive evidence of the impact of exposure biomarker feedback in a general population sample (Barnfather 2005) has been criticised for methodological flaws (Stapleton, 2005; Coleman, 2005) and thus results from the study need to be cautiously considered given this background.

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<sup>18</sup> In contrast to Burling 1991 and Cope 2003, Audrain 1997 found no significant effect for exposure feedback vs. no feedback on smoking cessation or reduction in a non-pregnant population

The application of harm biomarkers also yielded somewhat ambiguous results but tended to support their use in interventions. One study (Shahab 2007) was underpowered to detect anything but very large effects, and of the remaining two studies one (Segnan 1991) found no evidence of an effect and the other (Bovet 2002) reported a significant increase in cessation rates. The latter study, despite having one of the shortest interventions, produced one of the strongest results. In contrast to the Segnan study, which used spirometry results to represent harm, Bovet *et al.* (2002) relied on the influence of the concrete visualisation of harm exposure on smoking cessation. Although there was no significant impact of an intervention using the same visual harm biomarker feedback as Bovet *et al.* (2002) on cessation in the study by Shahab *et al.* (2007), there was an increase in perceptions of susceptibility to smoking-related harm.

The positive impact of visual harm biomarker feedback can be linked to literature on anxiety, imagery and coherence. Evidence suggests that anxious states promote concrete, spatial processing (visual) and inhibit verbal (abstract) processing of information (Gray, 2001), which implies that patients are more likely to comprehend, or take in, information presented in visual as opposed to abstract form. Visualisation has also been linked to increased emotional processing<sup>19</sup>. The anxiety provided by feedback may therefore facilitate the integration of particularly imagery laden illness representations (Cameron, 2003). In addition, the presentation of a concrete image of the negative effects of smoking may increase coherence, i.e. people's understanding of the link between smoking and its physiological effect on the body, since the connections between smoking and, in this case, heart disease, may not be very clear (Hall, Weinman,

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<sup>19</sup> The term emotional processing denotes a process whereby emotional disturbances are absorbed, worked through and decline to the extent that other experiences/behaviour can proceed without interruption (Rachman, 1980); this means information is properly integrated into cognitive structures, which will then result in appropriate behavioural adjustment, as has been shown in exposure therapy (Barlow, 1988)



& Marteau, 2004) therefore motivating behaviour change more effectively. However, some caveats regarding the included research on harm biomarker feedback need to be mentioned. As stated above, one of the studies reviewed had a very small sample size, which leaves open the possibility of Type II error confounding results. Moreover, the study that found a significant effect was carried with a sample of light smokers from a developing country and thus results may not as easily translate to other settings.

In contrast to both exposure and harm biomarker feedback, the evidence of the effect of susceptibility biomarker feedback on smoking cessation is much less ambiguous. The two studies in this review that looked at this issue did not detect a significant improvement in cessation after providing genetic risk feedback compared with a control condition. This finding is perhaps not surprising. Not everyone will have measurable genetic expressions of vulnerability and for those who have, common perceptions of immutability of genetic risk may reduce motivation to change behaviour; thus both these outcomes may reinforce smoking (Marteau & Lerman, 2001). Another issue of concern is the effect of susceptibility feedback on depression. There is a well-known association between smoking and depression (Fergusson, Horwood *et al.*, 1993) - it is feared that negative feedback may increase helplessness and affect smokers' emotional well-being (Croyle, Achilles, & Lerman, 1997). Fortunately, none of the papers showed any effects of biomarker feedback on depression at follow-up.

Finally, it is thought that a larger number of biomarkers may be more effective given the heterogeneous nature of smokers (McClure, 2001). However, this presumption was not entirely supported by the reviewed evidence. Although there was a tendency of studies with more biomarkers to increase cessation, and do so for a longer period of time, evidence suggests that just one biomarker may be as successful as many in reducing

smoking. Although the study (Richmond 1985) that employed more biomarkers than any other study produced the most significant effect, it also suffered from a number of methodological flaws including an incomplete matching of contact time between control and intervention conditions, thus the utility of feedback from several biomarkers cannot be unanimously supported by the reviewed studies.

Only very few studies considered the influence of moderating variables on outcomes; one variable important in this analysis was the level of education, which either directly (as observed in Bovet 2002) or indirectly (as shown by better study outcomes in populations with lower educational attainment) impacted cessation rates. The observed results are contradictory to findings reported elsewhere (Pierce, Fiore, Novotny, Hatziaandreu *et al.*, 1989), which show the opposite pattern: that is, smoking cessation is associated with a higher education level. It could be speculated that other variables, which relate to pre-existing perceptions and the way the information was presented, may have affected the result such that in this analysis, participants with lower education prior to the intervention may have been less aware of the detrimental health effects of smoking, resulting in a greater overall effect of the intervention.

Another set of moderating variables, fear and perceived susceptibility, were significantly associated with biomarker feedback. This may provide an insight into underlying mechanisms of behaviour change. Experiencing fear and increased susceptibility may add to the list of reasons to take health-protective action, essentially turning affect into cognition (Petty, Cacioppo, Sedikides, & Strathman, 1988), thus keeping the issue of cessation more salient. Alternatively, the emotional arousal of fear/feeling susceptible may directly promote coping (Easterling & Leventhal, 1989); as people want to manage this aversive effect, the way to control fear would be to do

something about the threat that is causing it, i.e. quit smoking (this is explored in greater detail in Chapter VII).

It has been stressed that the awareness of a preventable health hazard is an important determinant of behaviour change (e.g. Becker, 1974) and while it led to reductions in consumption and increased quit attempts, in the majority of the interventions it was not enough to improve cessation rates. Perhaps minimal contact approaches may not be intensive enough to change behaviour (Orleans, Schoenbach, Wagner, Quade *et al.*, 1991), and this is in part confirmed by this review as longer and more complex interventions tended towards better cessation outcomes. In particular, repetition of feedback may be important for increased cessation as this gives an opportunity to provide evidence of the amelioration of tobacco-inflicted harm or exposure as has also been observed elsewhere<sup>20</sup>. However, in agreement with other research, showing that minimal and more directed intervention programmes may be just as effective (e.g. Ockene, 1987), this review also found evidence of effectiveness in relatively minimal interventions.

#### **III.vi.i Limitations**

Addressing the initial questions of this review, it is important to return to the methodological concerns raised earlier. The quality of the assessed papers varied from studies being underreported, featuring poorly matched control conditions and high attrition (Cope 2003) to having well-matched control conditions, with low attrition rates (Bovet 2002) and providing extensive analyses (Audrain 1997). These variations may not only explain the differences in results but also somewhat limit the generalisability of the reported findings. Indeed, there was significant heterogeneity (or rather a lack of

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<sup>20</sup> Repeated cholesterol screening and feedback contributes to decreased total cholesterol levels (Burckett, Southard, Herbert, & Walberg, 1990)

homogeneity) in study results, which limits the utility of meta-analytic procedures such as pooling. While this review used random effects models to adjust for heterogeneity of results where this was present, it should be noted that this procedure is not necessarily able to yield meaningful results in all cases and is therefore considered inappropriate by some statisticians (see Higgins & Green, 2005). Another limitation arises from the search procedure; this review did not search specific grey literature databases, and the search was carried out by only one person and not validated by a second reviewer. However, the inclusion of PsycINFO as one of the databases searched does address the first issue to some extent since there is considerable overlap between PsycINFO and databases that focus on grey literature specifically. Moreover, the standardised procedure of data extraction using a specifically developed form should have reduced the possibility of overlooking relevant information. Lastly, the review – in contrast to Cochrane reviews – included studies with a shorter follow-up period and non-biochemically verified outcomes. Although this may reduce the reliability of results, it was hoped that less stringent inclusion criteria would overcome publication bias to some extent (which tends towards large trials with significant results) by also considering smaller trials with non-significant outcomes.

#### **III.vi.ii Conclusion**

Bearing these limitations in mind, it seems that cessation programmes with biomarker feedback can improve some smoking outcomes, i.e. reduce smoking and increase quit attempts, when compared with standard interventions, but they are much less effective for attainment of long-term cessation. While the majority of moderating variables assessed did not provide unambiguously significant results, there is evidence that biomarker feedback has a larger impact in less educated populations. There was also an effect of time and nicotine dependence on cessation rate. No conclusions could be reached with regard to which biomarker is most effective. As results from the included

studies were too heterogeneous, it is impossible to come to an ultimate conclusion about the overall utility of biomarker feedback. Nonetheless, it seems that the application of both exposure and harm biomarkers can improve cessation rates, though the former may be only effective in highly-motivated populations such as mothers-to-be, and the latter yet needs to be tested in a population with more dependent smokers. In terms of the structure of the interventions assessed, no single design was consistently related to better outcomes, and the use of multiple biomarkers does not appear to improve outcomes compared with single biomarkers. Indeed, for the sake of pragmatism and simplicity, interventions should be easy to conduct, cost-effective and time efficient. Short interventions, which employ only one biomarker and still produce significant result, as was the case in Bovet's *et al.* paper, are therefore particularly useful.

In consideration of this review, future research ought to raise methodological quality to a higher and more uniform level in order to clarify contradictory study results. Studies are required to improve on matching between treatment and control conditions, to have an adequate sample size, to utilise appropriate randomisation procedures and analytical techniques (such as intention-to-treat). This review would thus support the conclusion of an earlier meta-analysis (Bize, Burnand *et al.*, 2005) that 'there is a scarcity of evidence of sufficient quality' and that 'no definitive statements about the effectiveness of biomedical risk assessment as an aid for smoking cessation' can be made. However, in contrast to Bize *et al.* - but keeping the aforementioned limitations in mind - this review would suggest that there exists some limited utility for both exposure and harm biomarker feedback in motivating smokers to quit. For future research, it would be worthwhile to explore further the effects of fear and explicit harm imaging on cessation, perhaps by adding cognitive-behaviour therapy elements to interventions. Finally, considering the intricate and technical nature of the biochemical feedback that is

### Chapter III: Systematic review – biomarkers in smoking interventions

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involved, future studies testing such interventions ought to include measures to establish whether participants have actually understood the information provided, or at the very least provide additional written information about the feedback given, as only then is it possible to ascertain that it is biomarker feedback, and not how or by whom the feedback is provided<sup>21</sup>, which instigates behaviour change.

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<sup>21</sup> Both the conveyor of a message and the way it is framed have been shown to influence attitude change (Hovland, Janis, & Kelley, 1953)

## Chapter IV

### **Scope of the thesis: smoking-related biological markers and smoking cessation**

#### ***IV.i Overview***

As outlined in the first two chapters, smoking prevalence has been greatly reduced since the 1970s, at least in most developed countries, and biomarkers have been instrumental in furthering tobacco control. Chapter III more specifically investigated the utility of smoking-related biomarkers when added to smoking cessation interventions and found some limited evidence for their efficacy. However, as was previously stated, from the mid 1990s onwards the decline in national smoking rates in the UK started to slow, and prevalence over the last ten years has fallen by roughly 3% compared with approximately 6% over the previous ten years (Goddard, 2006). What is more, the smoking prevalence in many developing countries is increasing, in part due to shifting perceptions regarding smoking among women, and in part due to a relatively underdeveloped tobacco control lobby that is faced by the aggressive expansion of tobacco companies in these countries.

Consequently, there remains a need for a continued effort to improve tobacco control. As Chapter II highlighted, one option is to make more use of the large range of biological markers of smoking-related exposure, risk and harm to support tobacco control strategies. Owing to their versatility, biomarkers have proven useful to virtually all aspects of tobacco control, but for obvious reasons, it would be beyond the remit of this thesis to investigate novel applications and uses of biomarkers for every area of tobacco control. In light of this, the current thesis will primarily focus on the role of smoking-related biomarkers in smoking cessation by making use of the whole breadth

of biomarkers available, i.e. those evidencing exposure and risk as well as those indicating harm.

### ***IV.ii Summary of thesis research***

As stated before, the overarching aim of this thesis is to broaden our understanding of the utility of smoking-related biomarkers in tobacco control, with particular reference to smoking cessation programmes. The following chapters will therefore address a diverse set of research questions: from whether we need biomarkers at all to how biomarkers could improve intervention outcomes; from why the application of biomarkers is especially important for those smokers who have already developed smoking-related diseases (and thus are at most risk) to what smokers think of this approach to aid smoking cessation.

As argued in Chapter I, tobacco control may best be defined by the realm of action that it occurs in. Slama (2004) argues this primarily involves strategies that are based on legislation and policy; on basic research, public awareness and values or on intervention programmes. Biomarkers have contributed to each of these action domains in tobacco control as outlined in Chapter II. This thesis will therefore follow Slama's approach by elucidating the role of smoking-related biomarkers in the three areas of action while maintaining a specific focus on smoking cessation. Each study investigated at least one of each biomarker type to advance our knowledge of the utility they have for tobacco control today; exposure biomarkers are evaluated in studies 1 through 3; risk biomarkers<sup>22</sup> in studies 2, 3 and 5 and harm biomarkers in studies 2, 4, and 5. Study 1 assesses the use of biomarkers for the evaluation of legislation and policy changes, and studies 2 and 3 look at the role of biomarkers in smoking cessation interventions. Lastly, studies 4 and 5 provide evidence of the importance of biomarkers in basic

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<sup>22</sup> Expired air carbon-monoxide is considered both an exposure as well as risk biomarker



tobacco control research and for raising public awareness. The order of studies was chosen to reflect the area of action that is considered as well as the methodological approach used in each study – from a small scale, individual focus to a large scale, broad impact perspective. While more specific aims and objectives are provided at the beginning of each chapter, the following section will briefly outline the studies which form part of this thesis and how these contribute to the overall investigation of the role of smoking-related biomarkers in smoking cessation.

### **IV.ii.i Study 1**

One obvious first question one may ask when considering smoking-related biomarkers is how useful they really are. In particular with regard to biomarkers of exposure, it is possible to imagine easier, less time-intensive and thus cheaper options to assess smoking, namely self-report. Study 1 therefore evaluated whether exposure biomarkers can be replaced by self-report and compared self-reported puffing behaviour (as a measure of the degree of exposure) with actual exposure to tobacco smoke, which was determined by salivary cotinine levels. This study thus enabled a look at whether or not biomarkers are essential for evaluating the impact of policy changes and new legislation (e.g. tax increases, introduction of emission limits).

### **IV.ii.ii Study 2**

An important, initial question in the context of biomarkers and smoking cessation is how smokers progress towards cessation and what smokers think not only of existing interventions (such as provided by the NHS Stop Smoking Services) but also about the incorporation of biological markers in novel smoking cessation interventions. One possible approach to generate new theoretical insights into the process of smoking cessation, and to inform existing as well as future interventions, is to look at these issues with different, generative research methodologies. For this reason, Study 2 used an

exploratory, qualitative approach to chart the progression from being a smoker to stopping smoking by interviewing smokers who had never tried to quit smoking, smokers who had attempted to quit but had failed and those who had successfully managed to stop smoking. In addition to assessing participants' views of current interventions (smokers who had successfully or unsuccessfully attempted to stop smoking had gone through the NHS Stop Smoking Services), the interview also probed smokers' and ex-smokers' attitudes towards the use of biological markers as an addendum to existing interventions.

### **IV.ii.iii Study 3**

Despite using different methodologies, both the meta-analysis presented in Chapter III and the qualitative analysis in Study 2 found some evidence to suggest that expired carbon-monoxide feedback<sup>23</sup> may help motivate smokers to stop. Study 3 therefore evaluated the effectiveness of adding feedback of expired carbon-monoxide levels to brief smoking cessation advice using a randomised controlled trial design. In order to determine which processes underlie the potential impact that biomarker feedback may have on smoking cessation, this study also assessed a number of cognitive variables that have been suggested as instrumental for health promotion interventions in general and fear appeal interventions, such as this, in particular.

### **IV.ii.iv Study 4**

The last two studies expanded the focus of this thesis by looking at the role and importance of smoking-related biomarkers for smoking cessation in relation to specific diseases from an epidemiological perspective and thus highlight the utility of biomarkers in basic research to raise public awareness of pertinent issues.

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<sup>23</sup> In the meta-analysis, this finding more generally applied to exposure biomarkers, and CO feedback was found to be effective in comparison with minimal interventions only

As indicated in Chapter I, chronic obstructive pulmonary disease is one of the most common diseases associated with smoking and results in numerous preventable deaths each year. Study 4 used data from the Health Survey for England to fill a gap in current knowledge by providing up-to-date national prevalence estimates of smoking rates among people with objective signs of COPD determined by spirometry, a biomarker of smoking-related harm that assesses lung function. This study further evaluated the level of under-diagnosis among people with objective signs of COPD as well as the impact of receiving a diagnosis with COPD on smoking rates and smoking cessation.

### **IV.ii.v Study 5**

Another disease (or rather set of diseases) discussed in Chapter 1 that represents a major contributor to premature disability and death among smokers is cardiovascular disease. Study 5, like Study 4, used data from the Health Survey for England to provide up-to-date smoking prevalence estimates among people with CVD and/or CVD risk factors. Further, using biological markers of smoking-related risk and harm that are implied in CVD development (blood pressure, blood lipids, fibrinogen etc.), this study investigated the level of detection of CVD and CVD risk factors in the population. The analysis also evaluated the impact of receiving an appropriate disease diagnosis on smoking cessation among people with objective signs of a CVD-related disease (such as hypertension, diabetes, metabolic syndrome).

The studies in this thesis thus endeavor to evaluate the role of smoking-related biomarkers in smoking cessation from a variety of angles and contexts (small scale/experimental and large scale/observational) as well as methodologies (qualitative and quantitative) in order to provide as comprehensive an analysis of the utility of biomarkers in this area of research as is feasible for the remit of a PhD.

## Chapter V

### Study 1: The reliability and validity of self-reported puffing behaviour<sup>24</sup>

#### ***V.i Introduction***

Self-reported smoking status is generally thought to be a relatively good indicator of biomarker-validated smoking status (Patrick, Cheadle, Thompson, Diehr *et al.*, 1994), although there is evidence that self-report may in fact substantially underestimate smoking prevalence in some countries (West, Zatonski, Przewozniak, & Jarvis, 2007). The fact that self-reported smoking status is a relatively reliable proxy for biomarker-validated smoking status allows for the easy assessment of smoking prevalence in large nationally representative samples through standardised questionnaire items. In addition, smoking status and the number of cigarettes per day are only crude indicators of tobacco consumption and intake. There is significant variation among smokers in the intensity with which each cigarette is smoked, so that some smokers inhale two to three times more smoke than others smoking the same brand (Hammond, Fong, Cummings, & Hyland, 2005). Smokers adjust the number, size, and speed of their puffs to extract the desired amount of nicotine (Benowitz, 2001). As a result, roll-your-own smokers take more and longer puffs to overcome greater resistance of less ventilated and more densely packed hand-rolled cigarettes in comparison with manufactured cigarettes (Shahab, West, & McNeill, 2007) and manufactured cigarette smokers who switch to cigarettes with lower machine measured tar and nicotine yields compensate for lower nicotine delivery by smoking cigarettes more intensively to maintain a relatively constant level of nicotine in their body (Benowitz, Jacob, III, Kozlowski, & Yu, 1986; Bridges, Combs, Humble, Turbek *et al.*, 1990; Djordjevic, Hoffmann *et al.*, 1997). Estimates of inhalation and puffing patterns would not only provide more reliable

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<sup>24</sup> A version of this study is currently in press (see Appendix V.V)

measures of intake but they are also critical to understanding the impact of different cigarette designs and thus exposure of smokers to toxins.

### **V.i.i Rationale**

The technology to measure puffing behaviour has improved with the advent of portable, hand-held devices (Henningfield, Yingling, Griffiths, & Pickens, 1980). However, measuring puffing topography remains a relatively costly, involved procedure that may not be feasible for large population-based studies. If this information could be collected with sufficient accuracy via self-report, it would make studying puffing behaviour in population samples much easier. Yet, to date few studies have examined the extent to which smokers can provide accurate self-reports of their puffing behaviour. What research exists provides conflicting findings. For example, self-reported inhalation was found to be significantly associated with biological markers of nicotine intake in some (Burling, Lovett, Richter, & Frederiksen, 1983; Hofer, Nil, Wyss, & Battig, 1992; Nakayama, Yokoyama, Yoshiike, Ichimura *et al.*, 1999), but not other studies (Frederiksen, Martin, & Webster, 1979; Hill, Haley, & Wynder, 1983; Etter & Perneger, 2001).

Validated measures of self-reported puffing behaviour would be particularly valuable for assessing individual variation in nicotine dependence, which could be useful for treatment planning, as well as for measuring compensatory shifts in response to tobacco control policies, such as increases in cigarette prices or taxation. For example, although tax/price increases have been demonstrated to reduce the number of cigarettes smoked (Jamrozik, 2004), it is not known whether smokers compensate by smoking each cigarette more intensely, although there is good reason to believe that this is the case (e.g. see Ahijevych, Weed, & Clarke, 2004; Adda & Cornaglia, 2006). If each cigarette is smoked “harder”, there may be little or no decrease in overall exposure resulting in a

smaller than expected impact of taxation on health differentials. In addition, differences in puffing behaviour in terms of demographic or smoking characteristics may provide valuable insights into socio-demographic determinants of risk-exposure, smoking reduction and cessation. For instance, recent studies have reported significant differences in machine-assessed puffing behaviour between men and women (Eissenberg, Adams, Riggins, III, & Likness, 1999; Wood, Wewers, Groner, & Ahijevych, 2004; Hammond, Fong *et al.*, 2005).

As part of an international collaboration assessing exposure to smoke constituents, this study therefore sought to assess the value of self-reported puffing behaviour as a tool to estimate smoke intake over and above biological markers of intake. Self-reported puffing was compared with machine-determined smoking topography and other smoking-related markers to examine its reliability and validity.

### **V.i.ii Aims**

Specifically, the aims of this chapter were to:

- 1) Assess the stability of self-reported puffing behaviour over a 24 h period compared with machine-determined puffing behaviour.
- 2) Determine the correspondence, if any, between equivalent self-reported and machine-determined measures of puffing behaviour.
- 3) Evaluate the association between self-reported puffing behaviour and markers of smoke exposure.

### **V.ii Methods**

#### **V.ii.i Participants**

Participants were recruited through advertisements in local newspapers, flyers, emails, or posters on public bulletin boards at five different sites, across four countries: Waterloo, Canada; Melbourne, Australia; London, UK; and Buffalo and Minneapolis,

US. Smokers who responded to the advertisements were screened for eligibility through a telephone interview. Participants were included if they were between 18 and 50 years of age, smoked at least ten cigarettes daily for the past year and had been a regular smoker of one particular cigarette brand for more than 3 months. Seventeen eligible cigarette brands were selected on the basis of national sales and nicotine yield, between three and five brands from each country. At least one of the most popular 'light' and 'regular' cigarette brands in each country was included. Smokers were ineligible if they had a history of lung or heart disease or if they were pregnant. Ethical approval was sought and granted by local ethics committees at participating study sites based on ethical approval obtained at the main study site (see Appendix V.I).

### **V.ii.ii Procedure**

Participants visited the laboratory on two occasions, 24 hours apart and were instructed to abstain from smoking at least half an hour before each visit in order to standardise conditions. At the first visit, the purpose of the study was explained and consent obtained (see Appendix V.II for consent form); at both visits, participants were then asked to provide information about their smoking behaviour before saliva samples were collected. Between visits, participants were asked to continue smoking as usual and at the end of each session, participants smoked a cigarette through the CReSSmicro<sup>®</sup> machine (Plowshare Technologies, Inc. Baltimore, Maryland) to determine smoking topography. Participants were also provided with a container and asked to collect all the butts from the cigarettes they smoked in the 24 hours between the laboratory sessions. The box contained a pencil and a watch for participants to note the time of the cigarette on the appropriate tin. Participants were reimbursed the equivalent of \$50 USD for their time.

### **V.ii.iii Measures**

#### **V.ii.iii.i Demographic and smoking characteristics**

During the interview smokers were asked about their smoking history, quit attempts, future quit plans, as well as general demographic information (see Appendix V.III for questionnaire). Questionnaire items were used to calculate the Heaviness of Smoking Index (HSI, Heatherton, Kozlowski, Frecker, Rickert *et al.*, 1989) a short version of the Fagerström test for nicotine dependence. The HSI is derived from the time to the first cigarette ( $\leq 5$  min=3 points; 6-30 min=2 points; 31-60 min=1 point;  $>60$ =0 points) and cigarettes per day (1-10=0 points; 11-20=1 point; 21-30=2 points;  $>30$ = 3 points) producing a scale from 0 to 6 with higher scores indicating greater dependence on nicotine.

Cigarette brands were characterized by standard ISO/FTC nicotine yields rather than brand name (e.g. Light/Mild/Regular, etc.) due to country differences that exist in terminology. Percent filter ventilation, an indicator of the degree of air dilution in cigarette smoke produced by the ventilation holes in cigarette filters, was measured with a KC-3 digital apparatus (Borgwaldt-KC, Richmond, VA, USA) following an established protocol (Kozlowski, Mehta, Sweeney, Schwartz, Vogler, Jarvis, & West, 1998).

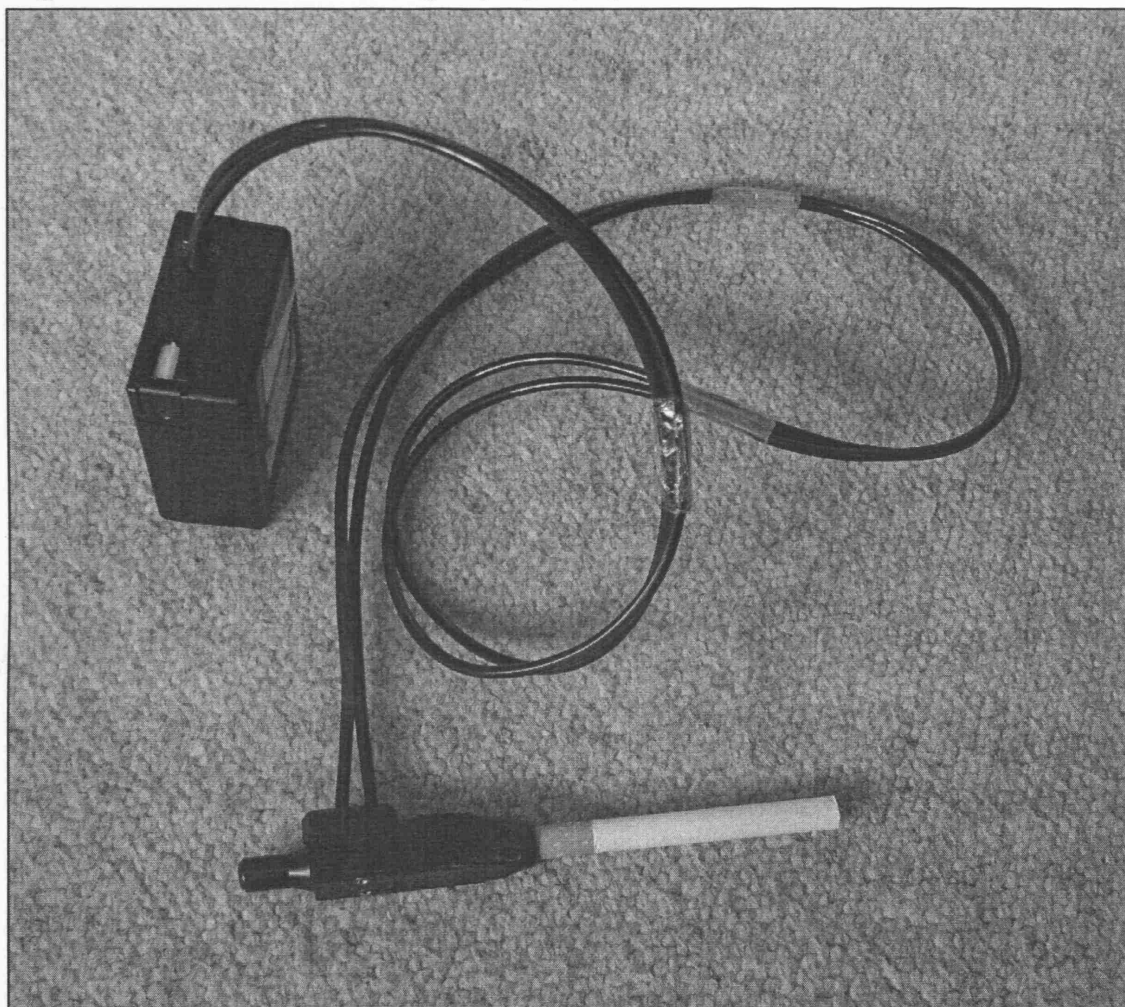
#### **V.ii.iii.ii Machine-determined puffing behaviour**

The CReSSmicro<sup>®</sup> machine is a battery-operated, hand-held portable device that measures a full complement of smoking topography variables including puff volume, puff count, puff duration, peak flow, inter-puff interval, time, and date (see Figure I.I). The device uses an orifice flow meter mouthpiece that produces a pressure drop related to the flow rate of smoke through the mouthpiece. Data are collected by having the participant insert a cigarette in the device and smoke the cigarette as normal. Once the



participant has finished, the cigarette butt is withdrawn from the device and extinguished, as usual. Data are stored on the device until downloaded for analysis.

**Figure V.I: Portable smoking topography device**



### **V.ii.iii.iii Self-reported puffing behaviour**

Four different self-report measures of smoking behaviour were assessed in a self-administered questionnaire (see Appendix V.III for questionnaire). This included: 1) inter-puff interval, assessed by asking smokers how long on average they let the cigarette burn in between taking puffs; 2) number of puffs per cigarette, determined by asking smokers if they: (a) take a few puffs on each cigarette, (b) take more than a few puffs but not as many as they could or (c) take as many puffs as they can on each cigarette; 3) depth of inhalation, determined by a single multiple choice item. Smokers were asked if they: (a) do not inhale into the chest at all, (b) inhale only a little into the

chest, (c) inhale deeply into the chest or (d) inhale into the chest as deeply as possible; 4) smoking intensity, assessed by asking smokers to indicate how 'hard' they smoked cigarettes on average on a scale from 1 (not at all hard) to 10 (as hard as possible).

### **V.ii.iii.iv Markers of smoke intake**

#### *Filter butt measures*

Smokers' cigarette butts were analysed for solanesol using liquid chromatography and tandem mass spectrometry at the Center for Disease Control in Atlanta, USA (Watson, McCraw, Polzin, Ashley *et al.*, 2004). Solanesol is a naturally occurring constituent of tobacco deposited in cigarette filter butts during smoking, which is related to the tar and nicotine delivery of cigarettes. Filter butt nicotine levels were derived from solanesol values using calibration curves that were developed from a series of machine smoking runs with varying puff number, puff volume, and filter blockage. Both average butt nicotine and solanesol levels were used as alternative filter-based measures of cigarette smoke exposure in the analysis.

#### *Cotinine*

Saliva samples were collected using a dental roll, which participants were asked to keep in the mouth until saturated. Samples were assayed for cotinine, a major metabolite of nicotine that provides a very sensitive and specific quantitative measurement of tobacco intake, using a tandem mass spectrometric method at the Center for Disease Control in Atlanta, USA (Bernert, Jr., McGuffey, Morrison, & Pirkle, 2000).

### **V.ii.iv Contributors**

The study was designed and carried out by an international group of researchers from Canada, the United States, Australia and the UK (see Publication in Appendix V.V for details of contributors). I was involved in the data collection at the UK site and am responsible for the conception, analysis and write-up of the study results pertaining to

the investigation of the relationship between self-reported and machine-determined puffing behaviour and their predictive utility for exposure to cigarette smoke.

### **V.ii.v Statistical Analysis**

Statistical analysis was carried out using SPSS 14.0. Parametric assumptions for continuous variables were examined by looking at histograms as well as the skewness and kurtosis of data<sup>25</sup> to assess normality of distribution and Levene's test to assess homogeneity of variance. Where variables failed assumptions, appropriate non-parametric tests were carried out. Test-retest reliability was evaluated by computing intra-class correlation coefficients (ICC) using a two-way mixed model. Pearson product moment correlation coefficients or Spearman's rho coefficients (for non-parametric measures) were used to assess the degree of association between and among the various self-report and machine-determined measures of puffing behaviour. To assess if the results remained consistent across various subgroups, stratified analyses were performed controlling for demographic and smoking history variables. Group differences were assessed by means of Chi-square or Mann-Whitney U tests for dichotomous and ordinal data, and t-test or ANOVA for continuous, normally distributed variables. In addition, within-subject changes across visits were determined with paired t-tests, and stepwise linear regression was conducted to assess associations between multiple predictors and outcome measures. Significance values were adjusted to account for multiple comparisons using the false discovery rate control (Benjamini & Hochberg, 1995).

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<sup>25</sup> Values between -1 and 1 were considered normal

### V.iii Results

#### V.iii.i Participant and country characteristics

A total of 157 smokers from four different countries participated in this study. Of these, 17 were excluded because they violated the study protocol (participants failed to return for the follow-up appointment, had smoked different cigarettes or had shared their CReSS machine with others) and 22 because some of their data were lost or missing due to machine failure. There were no significant differences between excluded and included participants on any of the demographic or smoking characteristics with the exception of quit attempts. Excluded participants were more likely to have attempted to quit smoking in the last 5 years than those included in the analysis (Fisher's Exact test,  $p=0.02$ ).

**Table V.I: Demographic and smoking characteristics**

	Australia (N=20)		Canada (N=18)		UK (N=26)		USA (N=54)		All Sites (N=118)	
<i>Demographic Characteristics</i>										
Mean (SD) Age	33.6	(7.0)	29.0	(9.4)	31.0	(7.2)	31.3	(10.0)	31.2	(8.9)
Percent (N) Male	55.0	(11)	77.8	(14)	53.8	(14)	50.0	(27)	55.9	(66)
<i>Smoking Characteristics</i>										
Mean (SD) Cigarettes per day	18.6	(6.7)	15.1	(4.6)	15.9	(5.9)	17.5	(4.9)	17.0	(5.5)
Percent (N) Smokers of brands <1 mg nic	55.0	(11)	11.1	(2)	100.0	(26)	37.0	(20)	50.0	(59)
Mean (SD) Heaviness of smoking index	3.1	(1.2)	2.5	(1.4)	2.5	(1.1)	3.2	(1.1)	2.9	(1.2)
Mean (SD) Years of smoking	17.0	(8.2)	12.7	(9.1)	13.6	(7.4)	14.3	(10.1)	14.3	(9.1)
Percent (N) Quit attempt in last 5 years	40.0	(8)	50.0	(9)	50.0	(13)	33.3	(18)	40.7	(48)
Median (range) Length of quit attempt in days	31.5 (0-356)		60.0 (3-510)		60.0 (1-420)		60.0 (2-270)		60.0 (0-510)	
Percent (N) Quit plans										
<i>Next month</i>	15.0	(3)	16.7	(3)	15.4	(4)	18.5	(10)	16.9	(20)
<i>Next 6 months</i>	25.0	(5)	22.2	(4)	34.6	(9)	22.2	(12)	25.4	(30)
<i>Beyond 6 months</i>	35.0	(7)	27.8	(5)	38.5	(10)	51.9	(28)	42.4	(50)
<i>No quit plan</i>	25.0	(5)	33.3	(6)	11.5	(3)	7.4	(4)	15.3	(18)

The 118 participants with complete data reported smoking a variety of eligible brands – the most popular brands in each country were: Marlboro Gold (61.5%, UK), Newport (38.9%, USA), Players Light (61.6%, Canada) and Peter Jackson Super Mild (40.0%, Australia). Across sites, half of participants smoked cigarettes with machine-based nicotine yields of 1 mg or above while the other half smoked cigarettes with machine-based nicotine yields below 1 mg, as determined by standard ISO/FTC testing protocols (see Table V.I) ; however, this differed by country ( $\chi^2(3)=40.7$ ,  $p<0.001$ ). In Canada significantly fewer participants smoked lower nicotine yield cigarettes than in any other country, whereas in the UK all participants smoked lower nicotine yield cigarettes, given regulatory limits in the EU.

ANOVA indicated a small difference between countries in the heaviness of smoking ( $F(3,113)=3.3$ ;  $p=0.024$ ); however, Tukey post-hoc analysis did not reveal significant disparities between specific countries, and there were no other significant country-level differences for demographic or any additional smoking characteristics. As shown in Table I.I, the average participant had been smoking for more than 14 years and currently smoked approximately 17 cigarettes per day. Just under half of participants had attempted to stop smoking in the last five years, and the majority of participants had no plans to quit in the next 6 months.

### **V.iii.ii Stability of self-reported compared with machine-determined puffing behaviour**

Test-retest reliability over a 24 hr interval for both self-report and puff topography measures are shown in Table V.II. Intra-class coefficients (ICCs) for all measures of self-reported general puffing behaviour were above 0.6 indicating that self-reported measures had fair-to-good or, when above 0.75, excellent test-retest reliability (Fleiss, 1986). Thus self-reported puffing behaviour - notwithstanding natural variability in

smoking topography - showed very similar stability over time compared with machine-determined puffing behaviour in this sample. Since test-retest reliability was established, and paired t-tests revealed no significant differences between visits on any self-report or CReSSmicro measure, further analyses were carried out using mean values across visits.

**Table V.II: Intra-class coefficients of puffing behaviour measures**

<i>Self-report</i>	ICC (95% CI)
Puffs per Cigarette	0.628 (0.505-0.726)
Inter-puff Interval	0.760 (0.672-0.827)
Inhalation Depth	0.773 (0.689-0.837)
Smoking Intensity	0.808 (0.735-0.863)
<i>CReSSmicro device</i>	
Puffs per Cigarette	0.466 (0.314-0.596)
Inter-puff Interval	0.498 (0.350-0.622)
Puff Volume	0.701 (0.597-0.783)
Peak Puff Flow	0.819 (0.749-0.870)
Average Puff Flow	0.810 (0.738-0.864)
Puff Duration	0.649 (0.532-0.743)

Table V.III shows the correlations among the four self-reported measures of cigarette puffing behaviours as well as among the six machine-determined measures of smoking topography, which tended in the anticipated direction underlining their reliability. As would be expected, among the self-reported measures, greater smoking intensity was associated with a larger number of cigarette puffs and a greater inhalation depth; the latter two measures were also positively correlated.

In line with expectations, self-reported inter-puff interval was negatively correlated with the number of cigarette puffs, though this was not significant ( $p=0.50$ ). In contrast, machine-determined puffs per cigarette were negatively correlated with machine-determined inter-puff interval as well as all other CReSSmicro parameters. Moreover,

being determined by peak and average puff flow as well as puff duration, puff volume was positively correlated with these measures and, as anticipated, a greater average puff flow was associated with a greater peak puff flow but - by off-setting the need to puff for longer - with a shorter puff duration.

**Table V.III: Correlations of self-reported and machine-determined puffing behaviour measures**

<i>Self-report</i>	Puffs per Cigarette <sup>§</sup>		Inter-puff Interval	Inhalation Depth <sup>§</sup>	
Inter-puff Interval	-0.063				
Inhalation Depth <sup>§</sup>	0.185*		-0.048		
Smoking Intensity	0.375**		-0.035	0.625**	
<i>CReSSmicro device</i>	Puffs per Cigarette	Inter-puff Interval	Puff Volume	Peak Puff Flow	Average Puff Flow
Inter-puff Interval	-0.555**				
Puff Volume	-0.416**	-0.142			
Peak Puff Flow	-0.181*	-0.066	0.567**		
Average Puff Flow	-0.905**	-0.057	0.399**	0.905**	
Puff Duration	-0.327**	-0.124	0.654**	-0.105	-0.305**

\* p<0.05 level, \*\*p<0.01 level, <sup>§</sup> Spearman's rho (elsewhere Pearson's r)

### **V.iii.iii Association between self-reported and machine-determined measures of puffing behaviour**

Self-reported measures of puffing behaviour were compared with machine-determined smoking topography to evaluate the content validity of self-report. The analysis indicated significant but weak correlations between some of these measures (see Table V.IV). This table includes two additional machine-determined variables, which represent composites of CReSSmicro measures – total smoke volume (puff volume x puff number) and total puffing duration (puff duration x puff number). These were calculated in order to provide some measure of smoking behaviour at the cigarette (as opposed to puff) level. Similarly, a compound measure of the self-report variables was

computed by adding average self-reported puffs per cigarette, self-reported inhalation depth and the reversely coded, categorised self-reported inter-puff interval (6 categories; lower interval limits in seconds: 0, 5, 10, 15, 20, 30) to obtain an equivalent overall measure of self-report with greater values indicating harder smoking of cigarettes. This measure was reliable (Cronbach's  $\alpha=0.88$ ).

**Table V.IV: Correlations between self-reported and machine-determined puffing behaviour measures**

		Self-report Measures				
N=118		Puffs per Cigarette <sup>§</sup>	Inter-puff Interval	Inhalation Depth <sup>§</sup>	Smoking Intensity	Self-report Compound
CReSSmicro Measures	Puffs per Cigarette	0.240**	-0.325**	0.118	0.032	0.397**
	Inter-puff Interval	0.015	0.395**	0.037	0.145	-0.370**
	Puff Volume	-0.072	-0.029	-0.022	-0.008	-0.070
	Peak Puff Flow	-0.077	0.013	0.007	0.001	-0.079
	Average Puff Flow	-0.069	0.008	0.043	0.063	-0.060
	Puff Duration	0.010	-0.050	-0.006	0.064	0.299**
	Total Puffing Duration (per cig)	0.201*	-0.283**	0.043	0.109	-0.021
	Total Smoke Volume (per cig)	0.170	-0.290**	0.065	0.043	0.282**

\*  $p<0.05$  level, \*\* $p<0.01$  level; <sup>§</sup> Spearman's rho (elsewhere Pearson's r)

As might be expected, the two measures of the number of puffs per cigarette were positively correlated. In terms of categorical self-report responses, smokers who reported taking more puffs per cigarette took a greater number of puffs as measured by the CReSSmicro device compared with people that reported taking fewer puffs; however, this difference was not significant ( $F(2,115)=2.8$ ,  $p=0.065$ ). The same applied to the total puffing duration per cigarette: smokers who reported taking more puffs per cigarette had a tendency to spend a longer time inhaling per cigarette ( $F(2,115)=2.5$ ,  $p=0.084$ ).



Although there was a significant correlation between the self-reported and machine-determined inter-puff interval ( $r=0.40$ ,  $p<0.001$ ), smokers on average underestimated the time they spent between taking cigarette puffs in absolute terms by about 5.2 seconds. While roughly one third overestimated and two thirds underestimated the inter-puff interval, only twelve participants correctly reported the time they spent between taking puffs to within two seconds. This difference between actual and perceived inter-puff interval was significant ( $t(117)=4.4$ ,  $p<0.001$ ). In addition, reporting a longer inter-puff interval was associated with a smaller total inhalation volume and a shorter inhalation duration per cigarette as recorded by the smoking topography device.

As can be seen in Table V.IV, there was some asymmetry in the relationship between self-report and CReSSmicro measures. Whereas the self-reported inter-puff interval was negatively correlated with the machine-determined puffs per cigarette, the machine-determined inter-puff interval was not significantly correlated with the self-reported puffs per cigarette. Moreover, smokers' self-reported depth of inhalation was not significantly correlated with puff volume, inhalation volume per cigarette or any other CReSSmicro measures. Although self-reported smoking intensity was also not related to any machine measures, including average and peak puff flow as would be expected, it was significantly correlated with the total time that people spend smoking a cigarette (i.e. sum of both the puffing time and inter-puff interval;  $r=0.24$ ,  $p=0.009$ , not shown). The compound self-report measure was significantly correlated with both the individual (though not the total) puff duration ( $r=0.29$ ,  $p<0.001$ ) and the total smoke volume per cigarette ( $r=0.28$ ;  $p=0.002$ ) suggesting some correspondence between overall machine-determined puffing behaviour and self-report.

Although the magnitude of some of the correlations between self-reported and machine-assessed puffing behaviours was reduced to non-significance when looking only at women as opposed to men, low-tar as compared to high-tar cigarette smokers and smokers with a low as opposed to a high HSI score, none of these group differences in correlation coefficients were statistically significant (all  $z$  scores  $< 1.96$ ). This finding was confirmed by further analysis. In order to systematically evaluate the possible influence of demographic or smoking characteristics, difference scores were calculated by subtracting self-report data from machine puffing data, either directly as for the inter-puff interval or using a  $z$ -score transformation to account for incompatibility in measurement scales. Stepwise multiple regression analysis predicting absolute values of these difference scores (i.e. the precision of smokers' estimates as compared to machine estimates) did not reveal any significant predictors.

### **V.iii.iv Puffing behaviour and measures of smoke exposure and intake**

In order to assess the construct or criterion-related validity of self-report, puffing behaviour measures were compared with two types of markers that self-report would be expected to be associated with: two filter-based exposure markers (solanesol and nicotine), and a biomarker of smoke intake (cotinine).

The compound variable was the only self-report measure associated with filter-based markers; it was marginally correlated with both average solanesol ( $r=0.20$ ,  $p=0.04$ ) and nicotine ( $r=0.18$ ,  $p=0.05$ ) levels. However, none of the self-report measures related to a biomarker of smoke intake, i.e. cotinine, in bivariate analysis. Stepwise linear regression was conducted to estimate independent effects of self-report on outcome variables. Controlling for age, sex, HSI and filter ventilation, the compound variable was the only significant predictor of average solanesol ( $\beta=0.20$ ,  $t=2.2$ ,  $p=0.027$ ) and nicotine levels

( $\beta=0.20$ ,  $t=2.2$ ,  $p=0.033$ ). In order to adjust for differences in metabolism, body mass index was added as a coefficient in the prediction of cotinine. However, only greater heaviness of smoking ( $\beta=0.43$ ,  $t=5.3$ ,  $p<0.001$ ) and age ( $\beta=0.39$ ,  $t=4.8$ ,  $p<0.001$ ) but not self-reported puffing predicted cotinine levels. These results were not significantly changed when ISO nicotine yield was included in the prediction model or when looking at Visit 1 and 2 cotinine levels separately.

### **V.iv Discussion**

This is the first multi-country study to investigate the reliability and validity of self-reported smoking topography. In agreement with previous research, machine-determined smoking topography indicates that people's puffing behaviour is relatively consistent for at least short periods (Lee, Malson, Waters, Moolchan *et al.*, 2003; Hammond, Fong *et al.*, 2005) and this study was able to show that self-reports of general puffing behaviour were equally stable confirming an earlier study (Etter & Perneger, 2001).

Self-reported measures of puffing behaviour were, by and large, weakly correlated with machine-determined measures in the expected direction – a longer reported inter-puff interval was related to a longer machine measured inter-puff interval, although there was a difference in absolute terms. Similarly, a greater number of self-reported puffs per cigarette was associated with a greater number of machine measured cigarette puffs. However, a greater self-reported smoking intensity was only related to a longer smoking duration and not a greater average or peak puff flow, indicating that smokers' interpretation of intensity may be more strongly linked to temporal than physical factors such as speed of inhalation. Consistent with previous research (Tobin, Jenouri, & Sackner, 1982; Hill, Haley *et al.*, 1983; Adams, Lee, Rawbone, & Guz, 1983), self-reported depth of inhalation was not correlated with machine-determined inhalation.

However, a composite of the self-report measures was significantly associated with the total puffing volume suggesting that smokers had some general understanding of their overall smoking topography. This relationship between machine and self-reported measures was not significantly influenced by any of the assessed demographic variables or smoking characteristics.

Self-reported puffing behaviour was also validated against a biomarker and two filter-based markers of nicotine intake so as to estimate the relationship between self-report and actual smoke exposure. The amalgamated measure was a consistent predictor of both filter-based cotinine and nicotine levels implying that the combination of self-report measures is potentially useful in capturing smoker's exposure to cigarette smoke - at least at the mouth level. In contrast, the analysis of self-reported puffing behaviour and cotinine levels showed that the measures used in this study bear little, if any, relation to actual smoke intake. This differs from a previous report, which found self-reported smoking intensity to be a good predictor of cotinine levels (Etter & Perneger, 2001). There are a number of possible explanations for this discrepancy. The current study used a different self-report measure, which assessed smoking intensity on a 10 point (as opposed to 100 point) scale and it might be that the Etter measure of smoking intensity ("Indicate, on a scale from 0-100, the intensity of your smoking") was better than this measure at capturing puffing behaviour. Moreover, the current study not only employed a different methodology to determine saliva cotinine values but also recruited participants at five sites in four different countries thus including smokers of a much broader and varied range of cigarettes, which may have introduced further noise into the data. Lastly, in contrast to Etter and colleagues, who received one saliva sample by mail, in the current study saliva samples were collected on two occasions in person at the same time of the day. As there can be some short and long-term variation in

smoker's cotinine levels (Davis & Curvall, 1999), this may have also contributed to the contradictory finding.

The association of self-report with mouth-level exposure to smoke, as measured by filter butt solanesol and nicotine, but not with a biomarker of smoke intake, cotinine, may be the result of a number of intervening factors. The bodily uptake of smoke constituents is dependent not only on inhalation behaviour but also on smoke chemical parameters, lung morphology and other physiological parameters such as vital capacity, rate of breathing and clearance of the lung (e.g. Darby, McNamee, & van Rossum, 1984). In addition, there is individual variability in the extent to which smokers metabolise nicotine to cotinine, which has been proposed to be contingent on genetic polymorphisms of the *CYP2A6* gene (e.g. Nakajima, Kuroiwa, & Yokoi, 2002; Malaiyandi, Sellers, & Tyndale, 2005). Moreover, while cotinine is a reliable marker of long term exposure to tobacco in absolute terms (Zevin, Jacob, Geppetti, & Benowitz, 2000), it may not be sensitive enough a marker of exposure to reflect differing puffing behaviour owing to its long half-life. This is, for instance, highlighted by the finding that cotinine measurements can not always differentiate between light, medium and heavy smokers (Binnie, McHugh, Macpherson, Borland *et al.*, 2004). These limitations in terms of the uptake of nicotine, metabolism to cotinine and clearance of cotinine and may at least in part explain why self-reported puffing behaviour was not related to cotinine despite smokers' ability to report their puffing behaviour with some validity.

### **V.iv.i Limitations**

This study has a number of limitations. The restricted relationship between objective and self-report measures could reflect the inherent difficulty of the self-report task: smokers may have limited awareness of their discrete smoking behaviours, or it could be that the questions that were asked to determine puffing behaviour - or the

combination of these questions - was sub-optimal. Self-reported and machine-determined puffing cannot be easily equated as the former was assessed with fairly crude questions that reflected “general” or “typical” puffing behaviour, while the latter related to two particular cigarettes. Moreover, the use of a smoking topography device itself could have caused some changes in people’s smoking behaviour thus undermining the association between self-report and machine measures. Although a previous study using this device concluded that it provides a reliable and valid index of conventional smoking (Lee, Malson *et al.*, 2003), some degree of reactivity cannot be excluded, especially as participants were not able to habituate to the machine having used it only twice. Given that smoking behaviour is known to be variable, this “snap-shot” measurement of smoking topography may therefore limit the conclusions that can be drawn based on machine measures alone. A final limitation concerns the sample selection; participants were self-selected, and this may have influenced the outcomes of the study by possibly introducing some uncontrolled confounders.

This study also had a number of strengths. It was able to replicate findings across several countries in a controlled setting using comparable procedures. Not only does this lend a degree of generalisability to the results that could not be obtained from a single country study but also confirms the viability of this approach. Indeed, cross-national studies will arguably become ever more important for tobacco control as tobacco companies pursue increasingly globalised strategies and policies.

### **V.iv.ii    Implications and conclusions**

These data suggest that more work still needs to be done before self-report of smoking topography can be used as a proxy for smoke exposure and intake. The consistency of both self-reported and machine-determined measures of smoking topography suggests basic underlying mechanisms determining how people smoke (i.e. nicotine addiction).

While self-report was shown to have good test-retest reliability and some content validity, in terms of its relationship to outcome criteria, it was only predictive of mouth-level smoke exposure and not actual smoke intake, and this may be due to unobservable factors.

Overall, the modest concordance between self-reported puffing behaviour and machine-determined smoking topography, filter butt solanesol and nicotine but not cotinine implies that smokers have only limited self-awareness of their actual puffing behaviour and nicotine intake, and more research is needed to see if questions with better sensitivity can be developed. In general, the results indicate that smokers have a greater understanding of the number of puffs and the time in between puffs rather than of the depth, strength or intensity of each puff. It is currently unclear whether smokers' self-perception of smoking topography is sensitive to changes in smoking behaviour over time – an area that requires further investigation. Given these restrictions, the findings suggest that self-reported puffing, as assessed in this study, has currently only limited utility for the evaluation of smoking topography and smoke exposure in international questionnaire studies (or surveys) of smoking behaviour and that biomarkers of smoke intake are not readily replaceable by self-report measures.

## Chapter VI

### **Study 2: A qualitative enquiry of the process of smoking cessation and smokers' and ex-smokers' views on smoking cessation interventions**

#### ***VI.i Introduction***

Considering the topic of this thesis, the role of smoking-related biomarkers in smoking cessation, one initial and important question is how people progress from smoking to non-smoking; that is, what is the process of smoking cessation? Related questions are: what type of intervention would be likely to accelerate this process, and can biomarkers be usefully employed in such interventions? Surprisingly, there is a dearth of contextualised information on smoking, and relatively little is known about the specific reasons why people start to smoke, quit and how they quit (Willms, Best, Taylor, Gilbert *et al.*, 1990). Likewise, although health psychology research has produced a plethora of models, which have been used to devise health-focused interventions (Armitage & Conner, 2000; Michie & Abraham, 2004), it is likely that there exist yet to be uncovered influences, which persist in impeding successful behaviour change (Kearney & O'Sullivan, 2003). Indeed, it has been argued that the advancement in the field of behavioural smoking cessation interventions has not been as fast or comprehensive as once expected (Piasecki & Baker, 2001).

While further progress can be made, effective behavioural interventions, of course, do already exist. In England, the country with the first national smoking cessation service (McNeill, Raw, Whybrow, & Bailey, 2005), there is comprehensive evidence that stop smoking services increase cessation rates compared with unaided quit-attempts (Alterman, Gariti, & Mulvaney, 2001; Stead & Lancaster, 2005). However, only about one in six attendees will actually maintain 12-months abstinence (Ferguson, Bauld,



Chesterman, & Judge, 2005) and although quantitative studies have provided us with a range of predictive criteria for quit success (e.g. see West, McEwen, Bolling, & Owen, 2001), there is currently rather limited information on the views of service users regarding the reasons for their success or failure to quit.

There has been plenty of debate about methodological aptness; which type of study should be used to answer which type of research question (Petticrew & Roberts, 2003). In view of the questions that this chapter poses with regards to the process of smoking cessation, smokers' and ex-smokers' views on existing as well as potential, novel interventions, it would seem that a qualitative approach is appropriate for a number of reasons. In contrast to quantitative methods, qualitative research is non-quantifiable, places its emphasis on meaning and takes a more naturalistic and holistic approach to scientific investigation (Strauss & Corbin, 1998). Qualitative methods therefore lend themselves to exploratory and generative rather than confirmatory and iterative research (Willig, 2001) and have consequently been advocated for both process evaluation (Muir Gray, 1996) and theory generation (Green & Britten, 1998). As a first step, qualitative research can provide an alternate source for theoretical guidance that could prove fruitful in the development of new and effective smoking cessation interventions (Erickson & Kaplan, 2000).

The advantages of qualitative research have slowly been recognised in tobacco control. In fact, it has been suggested that while there is no doubt about the effectiveness of most tobacco control approaches, the preponderance of quantitative methodology within this field has precluded more sophisticated insights into the relative role of tobacco control and consequently has lead to a somewhat overly simplistic view of the causal relationship between tobacco control approaches and tobacco use prevalence (Chapman,

1993). Despite the obvious advantage of using qualitative research to further our knowledge with regard to smoking and the best ways to encourage cessation, not many qualitative studies have been conducted in the field. A look at the literature of qualitative studies investigating smoking cessation reveals only a handful of reports. A systematic search with the broadest inclusion criteria that sampled all major search engines<sup>26</sup> produced less than twenty papers that explored smoking cessation to some extent in a qualitative study setting. A large number of these studies focused on adolescents and/or ethnic minorities and all except for one (White, Bush, Kai, Bhopal *et al.*, 2006) took place outside England.

### **VI.i.i Rationale**

Due to the nature of qualitative research, its epistemological and ontological stance, it is generally accepted that findings from qualitative studies have only limited generalisability, which is particular to their context and participants (Guba & Lincoln, 1982). Thus more qualitative research is required to investigate smoking cessation in a context specific to England. Asking smokers and ex-smokers to share their experiences of smoking cessation in general, and of the UK Stop Smoking Services in particular, may inform the future development of such services. However, as only a small proportion of the UK smoking population actually uses stop smoking services (in 2005/6 about six percent of UK smokers, Department of Health, 2006), it would also be worthwhile to explore what makes those smokers who attempt to quit with the Stop Smoking Services different in terms of their beliefs from those who have never attempted to quit smoking with the services. Within the broader context of tobacco control, it was argued in Chapter I that while the individual and intensive approach taken by the Stop Smoking Services will lead to a higher cessation rate than a

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<sup>26</sup> EMBASE, CINHAL, MEDLINE, Web of Science (SCI, SSCI, AHCI) and PsycINFO were searched combining two parameters, one relating to the study methodology (*qualitative*) and one relating to the study content (*smoking treatment* or *smoking intervention* or *smoking cessation*) in September 2007

population and more cursory approach (such as raising taxes), it will also reach fewer people and therefore have a smaller impact on overall smoking prevalence (Raw & McNeill, 1994). For this reason, less work- and time intensive smoking cessation interventions that reach more smokers - such as brief quit advice delivered by doctors during routine consultation – are of crucial importance for reducing tobacco use.

As described in Chapter III, there is some evidence that providing smokers with feedback using biological markers of smoking-related risk, exposure or harm can increase motivation to change behaviour in the face of health threats (McClure, 2001). As an addendum to brief smoking cessation advice, this type of intervention would have the potential to reach a large section of the smoking population and thus to have a sizeable effect in terms of motivating either cessation or attendance at current stop smoking services. However, before conducting large randomised controlled trials, the acceptability and potential effectiveness of such interventions using biomarkers would need to be assessed. In addition, new government guidelines demand a greater involvement of service users in both research and the development of new methodologies (Department of Health, 2001), and a qualitative study provides the ideal setting to investigate these issues. Face-to-face interviews are considered to form an important part of the evaluation of health interventions (Petticrew & Roberts, 2003), and this qualitative study attempted to gather insights about existing and future interventions from those people most knowledgeable about existing interventions (ex-smokers and smokers, who have already experienced smoking cessation interventions) and those, who are most likely to be targeted by future interventions (smokers, who have never attempted to quit).

### **VI.i.ii Aims**

The purpose of this qualitative study was therefore three-fold. First, it sought to explore how people go from smoking to non-smoking by comparing self-accounts of both people who had either never or at least once attempted to quit smoking and people who had been either successful or unsuccessful in their quit attempt. Second, this investigation aimed to elicit smokers' and ex-smokers' views on the current Stop Smoking Services, both among those who had never used the services and those who had attempted to quit with the help of NHS smoking cessation clinics. Third, this study intended to gather responses and reactions to interventions that involve biomarker feedback from people likely to benefit from such interventions.

### **VI.ii *Methods***

#### **VI.ii.i Participants**

Purposive sampling was used to recruit participants. This is a non-random method to ensure the inclusion of participants on the basis of key characteristics pertinent to the research question (Coyne, 1997). In order to be able to address the research questions, smokers and ex-smokers were recruited into one of three groups to fit the following characteristics:

- (a) Current smokers, who have never attempted to stop smoking
- (b) Current smokers, who have attempted to quit smoking with the help of the NHS Stop Smoking Service and have failed to achieve abstinence
- (c) Ex-smokers, who have attempted to quit smoking with the help of the NHS Stop Smoking Service and succeeded<sup>27</sup>

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<sup>27</sup> Ex-smokers had to have stopped smoking for at least 6 months to be included – this is because most relapses occur early on in quit attempts (Hughes, Keely, & Naud, 2004), and 6 months is usually considered an appropriate outcome for evaluating intervention effects (West, Hajek, Stead, & Stapleton, 2005)

## Chapter VI: Study 2 - Qualitative enquiry of smoking cessation

Between seven and eight participants per group were recruited, i.e. twenty-three in total (see Table VI.I for participant details). The sample size was thought to be appropriate as it followed recommendations for qualitative research by balancing attainment of relative diversity in the sample with the possibility of in-depth analysis (Ritchie, Lewis, & Elam, 2003). Sixteen participants attended NHS Stop Smoking Services, while the remaining seven participants were recruited from outside quit smoking services by means of 'snowballing'<sup>28</sup>.

### VI.ii.ii **Procedure**

Smokers and ex-smokers who had attended the Enfield and Haringey Stop Smoking Services at least 6 months ago were sent a letter of invitation to the study together with a participant information sheet (see Appendix VI.I). Those who returned a registration of interest form by Freepost were contacted and screened for their suitability<sup>29</sup> to take part in the study. Participants' queries regarding the study were also addressed at this stage. A suitable date, time and convenient location for the interview to take place (either at participants' homes, UCL or Stop Smoking Service premises) were then arranged. At the meeting, participants were given a brief background questionnaire assessing demographic variables as well as past and current smoking behaviour. This was followed by a 45-60 minute semi-structured face-to-face interview. Participants were asked to fill in a consent form at the start as well as at the end of the interview for the use of their tape-recorded interviews in the analysis (see Appendix VI.II). This was done in order to ensure that participants could make an informed choice in full consideration of the interview and the topics covered therein. Participants were also given another chance to discuss any worries or concerns, which may have arisen during

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<sup>28</sup> This is an opportunistic method of recruitment in which suitable participants are recruited through other participants, who are already in the sample; thus participants recruited through the NHS Stop Smoking Services were asked to refer any friends who had never attempted to stop smoking to the study

<sup>29</sup> Determined by location (within reasonable travel distance) and willingness to participate without reimbursement

the course of the interview. Finally, participants were asked if they knew any smokers, who had never attempted to quit smoking and would be interested in taking part in the study; these were then contacted and went through the same procedure as the other participants. However, smokers who had never attempted to quit smoking were also given information about available services to help them stop smoking.

This study received ethical approval from the involved NHS trusts (see Appendix VI.III).

### **VI.ii.iii Interview and topic guide**

The interview was semi-structured, using a topic guide that focused on five main areas: the participants' past smoking history, their attitudes towards smoking in general, their thoughts and/or experience of quit attempts, their views on the quit smoking services and their thoughts on a smoking cessation intervention involving biomarker feedback (see Appendix VI.IV for relevant topic guides). The topic guide was based on themes identified in a previous literature search (see Footnote 26) as well as on concepts derived from PRIME theory (West, 2006b), which proposes a motivational model that encompasses all levels of description (from reflexes, instincts, habits through to drives, evaluations and plans) to explain human behaviour – in particular as applied to addictive substances. For instance, one idea of PRIME theory is that changes in behaviour are not only influenced by planned but also by immediate chaotic processes, and therefore a question regarding the planning of quit attempts was included in the topic guide. A brainstorming session with those involved in the study (Robert West, Eleni Vangeli, and myself) was used to structure the topic guide to cover all aspects pertinent to the research questions. The topic guides for never, unsuccessful and successful quitters were refined and slightly altered on the basis of the fieldwork process in advance of the study to remove items that were not likely to generate germane responses.

## Chapter VI: Study 2 - Qualitative enquiry of smoking cessation

Semi-structured interviews using topic guides have several advantages over structured interviews; as the wording and order of questions is not dictated it affords more flexibility, which allows the interview to flow more naturally. It also enables the interviewer to adapt the level of language to the participant, tailor the wording as appropriate as well as to explore relevant issues not covered in the interview schedule when they arise. Interviewees were encouraged to speak freely and, if necessary, answers were probed further but sensitive topics, in so far as they were irrelevant to the research questions, avoided. Interviews were conducted in private rooms to ensure confidentiality and avoid unnecessary interruptions.

### **VI.ii.iv Questionnaire**

In order to contextualise responses, the background questionnaire assessed the following variables, which are known to impact on smoking behaviour as well as attitudes towards smoking:

- Demographic details (age, sex, education, employment, marital status)
- Fagerstrom test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991)
- Smoking status of partner (if applicable)
- Intention to quit (scale 1-5, from 'Not at all' to 'Very much indeed'; current smokers only)
- Craving for a cigarette (scale 1-5, from 'Not at all' to 'Very much indeed'; ex-smokers only)

The questionnaire for current and ex-smokers is provided in Appendix VI.V.

### **VI.ii.v Contributors**

This study was conceived, carried out and written up by myself. Eleni Vangeli and Robert West contributed to the preparation of the interview guide, and Eleni Vangeli assisted in the interpretation of data.

### **VI.ii.vi Analysis**

As Chamberlain (2000) rightly points out, in qualitative health research there is a danger to engage in ‘methodolatry’ – to put considerations regarding the precise method to be used above all other matters of interest. As qualitative researchers one can become a slave to procedure and be too concerned with following the proper and correct steps of various analyses rather than engaging in more important discussions about the philosophical assumptions of these approaches; qualitative research may thus be prone to avoid theoretical thinking and critical argumentation as well as presenting description at the expense of interpretation. Bearing this precaution in mind, the following paragraphs set out the rationale for, and principles of, the qualitative methodology adapted in this study, which largely follows Framework analysis (Ritchie & Spencer, 1994) but allows enough flexibility to veer from this approach where it was considered appropriate.

Tape-recorded interviews were transcribed *verbatim* into word documents to enable qualitative analysis (see Appendix VI.VI for a sample script). Grounded theory (Glaser & Strauss, 1967) was not judged to be appropriate for analysis as data collection was not driven by emerging theories until a point of data saturation. The meta-linguistic approach proposed by Discourse Analysis (Potter & Wetherell, 2007) was also considered inappropriate, as the social construction of smoking and smoking cessation was not one of the main topics of this study. Lastly, the current sample was thought to be prohibitively large for Interpretative Phenomenological Analysis to be carried out as this approach relies on a very in-depth analysis of only a small number of manuscripts of a single homogenous sample (Smith, 1996) whereas in this study, the sample was purposefully heterogeneous so as to be able to address the research questions.



Framework analysis can be applied to organise a large number of transcripts and has been designed specifically for use in social policy research. It is therefore particularly suited for this study, which – among other things – evaluated services users’ views on stop smoking clinics. Based on work by Hammersley (1990; 1992), it takes a ‘subtle realist’<sup>30</sup> stance regarding data and uses a pragmatic approach to the selection of analytic techniques thus allowing the researcher to mix quantitative and qualitative methods. This qualitative approach provides a rigorous and systematic methodology for analysis, which involves the creation of a thematic framework to classify and organise data according to key themes, concepts and emergent categories.

Framework analysis uses a matrix-based approach to thematic data organisation; through reading and re-reading of a subset of transcripts, emergent categories and concepts are identified and arranged into key themes, which are broken down into sub-topics. Once the framework is judged to be comprehensive, each key theme is displayed in its own matrix (or chart), in which every participant is allocated a row and each column denotes a different sub-topic. Data from each individual participant is then synthesised within the appropriate part(s) of the thematic framework – a process called “charting” (see Appendix VI.VII for an example chart). The initial process of developing a thematic framework by analysing a subset of transcripts involved two members of the team (Eleni Vangeli and myself) and charting was carried out by myself. This is an iterative process that required making changes to the framework as new transcripts were added. The final thematic framework was then checked against a

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<sup>30</sup> In terms of its ontological position, subtle realism assumes the existence of a social world that is independent of our understanding of it (in agreement with realism and in contrast to social constructivism). With regard to its epistemological position, subtle realism acknowledges that this social world - and multifaceted reality in general - can be accessed through interpretation (in agreement with phenomenology) and draws heavily on quantitative methods to ensure objectivity and neutrality in data collection while recognising possible sources of bias.

random selection of transcripts by two researchers (Eleni Vangeli and myself) to ensure reliability and validity.

Framework analysis aims to facilitate the search for explanations because of easy access to synthesised data (so that it can be continually revisited), the ability to look within individual cases across a range of themes and the ability to move effortlessly between theme- and case-based analysis because of the way that data are displayed in the matrix. Framework is also easy to implement in software and for the purpose of this analysis, transcripts were coded using Atlas.ti (© Scientific Software Development, Berlin), which enabled the identification of key themes and sub topics. A number of transcripts were double-coded by two researchers (Eleni Vangeli and myself) to ensure reliability. After all data had been charted, analysis began by providing descriptive accounts of the various themes that were identified. This was followed by a more in-depth examination of the charts to find salient associations between groups, key themes and social as well as demographic characteristics to develop typologies capturing the variation within data and to provide explanatory accounts of the patterns that emerged from the data. In order to avoid misinterpretation and ensure coherence of the exposition, discussions with colleagues and members of the research team were carried out throughout this analysis process.

One, perhaps troubling, issue for qualitative research is the assessment of the reliability and validity of the analyses that are carried out (Malterud, 2001). Following guidelines suggested for ensuring consistent quality when conducting and analysing qualitative research (e.g. see Mays & Pope, 2000), this study attempted to provide a clear, transparent exposition of methods (an audit trail). The interview schedules were also reviewed by an independent researcher to ensure their face validity and appropriateness,

and findings from this study were put in context of the literature to provide concurrent validity. Moreover, as indicated above, an independent audit was carried out by a researcher (Eleni Vangeli) to evaluate both the reliability and validity of conclusions and check for intrinsic coherence. Lastly, deviant case analyses<sup>31</sup> were conducted to scrutinise and refine interpretations.

### VI.iii Results<sup>32</sup>

#### VI.iii.i Description of sample

Characteristics of participants are shown in Table VI.I. Although groups differed somewhat, the study was not powered to detect significant effects, and thus data are provided primarily for descriptive, not analytic, purposes in order to situate the sample.

**Table VI.I Sample characteristics**

	Total Sample N=23		Group					
			Successful quitters N=8		Unsuccessful quitters N=8		Never quitters N=7	
Demographics								
Mean (SD) Age	43.9	(14.5)	45.8	(10.0)	50.6	(14.7)	34.1	(15.0)
Percent (N) Male	34.8	(8)	37.5	(3)	25.0	(2)	42.9	(3)
Percent (N) White	95.7	(22)	100	(8)	87.5	(8)	100	(7)
Percent (N) with Higher education	69.6	(16)	75.0	(6)	50.0	(4)	85.7	(6)
Percent (N) in Paid employment	60.9	(14)	62.5	(5)	50.0	(4)	71.4	(5)
Current/past Smoking								
Mean (SD) Cigarettes per day	19.7	(7.8)	24.4	(8.2)	17.2	(6.7)	17.1	(7.0)
Mean (SD) FTND rating	4.5	(2.6)	6.1	(2.6)	3.6	(2.5)	3.7	(2.0)
Mean (SD) Intention to quit/Cigarette craving	-		1.4	(0.5)	4.6	(0.7)	3.1	(1.1)
Percent (N) with partner who smokes	13.0	(3)	0.0	(0)	37.5	(3)	0.0	(0)

<sup>31</sup> Deviant case analysis stands for the systematic search of contradictory findings (or cases) in the explanatory account offered so as to challenge the interpretation and provide an alternative explanation for these findings

<sup>32</sup> From this section onwards, the following short-hand descriptors will be used for different groups: people who have never attempted to quit smoking are *never quitters*, people who have attempted to quit smoking but failed are *unsuccessful quitters* and people who have attempted to quit smoking and succeeded are *successful quitters*. *Successful* and *unsuccessful quitters* are defined as *ever quitters*.

The whole sample (as well as each group) was relatively well educated with over half of participants having attended university; the majority was in paid employment. There were more female than male participants. Never quitters were somewhat younger in comparison with ever quitters. Nicotine dependence (FTND) ratings were within the normal range and some retrospective bias may have been responsible for greater levels of self-reported dependence and number of cigarettes consumed per day among ex-smokers compared with current smokers.

### **VI.iii.ii Description of emergent key themes<sup>33</sup>**

After the initial coding of transcripts, recurring concepts were grouped into thirty-three sub-topics, which fitted into nine key themes that constitute charts 2-10 (see Figure VI.I). As would be expected, there were some similarities between issues addressed in the topic guide and the final thematic framework. While not all of the sub-topics were addressed in equal measure by successful, unsuccessful and never quitters, each of the key themes did feature in the accounts of members of all three groups.

Chart 1 provides background information and has been largely covered in Section VI.iii.i. Most of the participants who had tried to quit smoking (and had either succeeded or failed in their attempt) had tried to stop before – anything between one and over twenty times. Such previous quit attempts were rather varied in their outcome, some had managed to quit for only a couple of weeks whereas others had been abstinent for nearly five years. Information from Chart 1 was used in the development of typologies and to enable qualitative analyses of sub-groups. First, common emergent key themes across all groups will be presented before differences between groups are examined.

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<sup>33</sup> These themes were derived implicitly from responses that informed sub-topics in Charts 2 to 8; in contrast to themes in Charts 1, 9 and 10, which were derived from explicit questions

**Figure VI.I Thematic framework for analysis**

<p><b>Chart 1: Background</b></p> <ul style="list-style-type: none"> <li>&gt; Demographics (age, sex, education, employment, family structure)</li> <li>&gt; Smoking characteristics (previous quit attempts, nicotine dependence, current smoking status)</li> </ul>	<p><b>Chart 6: Triggers for quitting</b></p> <ul style="list-style-type: none"> <li>&gt; Extrinsic motivators</li> <li>&gt; Intrinsic motivators</li> <li>&gt; Health as motivator</li> </ul>
<p><b>Chart 2: Starting to smoke</b></p> <ul style="list-style-type: none"> <li>&gt; Intrinsically motivated start to smoking</li> <li>&gt; Extrinsically motivated start to smoking</li> </ul>	<p><b>Chart 7: Process of quitting</b></p> <ul style="list-style-type: none"> <li>&gt; Weary of quitting</li> <li>&gt; Quitting as challenge</li> <li>&gt; Quitting is easy</li> </ul>
<p><b>Chart 3: Positive appraisal of smoking</b></p> <ul style="list-style-type: none"> <li>&gt; Positive view / enjoyment of smoking</li> <li>&gt; Smoking to deal with stress</li> <li>&gt; Smoking as friend / shield</li> </ul>	<p><b>Chart 8: Smoking and Identity</b></p> <ul style="list-style-type: none"> <li>&gt; Dislike of smoking / smokers</li> <li>&gt; Transition in awareness / life-style</li> <li>&gt; Dissociation from smoking</li> <li>&gt; Identity / life-style not changed</li> </ul>
<p><b>Chart 4: Not owning up to smoking</b></p> <ul style="list-style-type: none"> <li>&gt; Smoking as norm</li> <li>&gt; Shifting responsibility</li> <li>&gt; Feeling naughty / rebellious</li> </ul>	<p><b>Chart 9: Stop Smoking Services (SSS)</b></p> <ul style="list-style-type: none"> <li>&gt; SSS positive views</li> <li>&gt; SSS negative views</li> <li>&gt; Group counselling is good</li> <li>&gt; Dislike of group counselling</li> <li>&gt; SSS improvement – structure/access</li> <li>&gt; SSS improvement - content</li> <li>&gt; SSS improvement - diversity</li> </ul>
<p><b>Chart 5: Negative effects of smoking</b></p> <ul style="list-style-type: none"> <li>&gt; Down-playing / derogating smoking-health risk link</li> <li>&gt; Addiction and need for aid ignored / down-played</li> <li>&gt; Awareness / acceptance of smoking-health risk link</li> <li>&gt; Addiction and need for aid acknowledged</li> </ul>	<p><b>Chart 10: Biomarker feedback</b></p> <ul style="list-style-type: none"> <li>&gt; CO testing scary but helpful</li> <li>&gt; Biomarker feedback helpful</li> <li>&gt; Problems with biomarker feedback</li> <li>&gt; Biomarker feedback – improvement</li> </ul>

### **VI.iii.ii.i Starting to smoke**

Participants recounted how they started smoking, and most of their stories centred on extrinsic reasons for taking up cigarettes. This included being influenced by family members and friends as well as by alluring images of smokers (as being cool and grown up). More often than not, participants mentioned peer pressure and trying to fit in as a motivation for early experimentation with cigarettes:

[I started smoking]<sup>34</sup> *because all my friends were trying it and I would have felt like the odd one out.* (P22, never quitter, female, age 26)

<sup>34</sup> Square brackets indicate paraphrasing

However, some participants also emphasised more internally anchored reasons for starting to smoke, such as curiosity:

*I was 16 [when I started smoking] and it was out of curiosity actually. (P20, never quitter, male, age 28)*

### **VI.iii.ii.ii Positive appraisal of smoking**

A positive attitude towards smoking was expressed both explicitly and implicitly in the accounts of a range of participants. Some were keen to stress their past or on-going enjoyment of cigarettes:

*I enjoy smoking. There are times when I think 'yeah I quite enjoy this'. (P18, never quitter, male, age 37)*

Other participants emphasised the utilitarian function that smoking has for them in terms of providing relaxation and dealing with stress:

*I think this started because I was a single mum and I'd moved away from a lot of friends and I'd got quite a stressful job and suddenly I noticed that I was buying a pack every other day and then that was it. (P5, unsuccessful quitter, female, age 45)*

For some participants, the cigarette even denoted something like a friend or a shield from the world providing a safe place to withdraw into their own:

*It was a friend, it wasn't just smoking [...] I enjoyed sitting back by myself having a cigarette. (P10, successful quitter, female, age 42)*

### **VI.iii.ii.iii Not owning up to smoking**

The third key theme that emerged from the data relates to participants' construal of responsibility regarding their current or former smoking. In particular, in terms of starting to smoke, participants were keen to point out that smoking was the norm for a long time, suggesting that not smoking would have violated some codex and that it was out of their hands:

*In fact, to be a non-smoker was more unusual at the time...in the early to mid 90s. (P16, successful quitter, female, age 33)*

Participants also provided a range of reasons why quit attempts had failed or not been carried out - most were related to external issues thus *de facto* shifting blame (and responsibility) for smoking to other people and to things out of their control:

*And people aren't always very supportive when you are trying to give up or they might sort of make fun of you. Some people will do that. (P14, unsuccessful quitter, female, age 44)*

*I've had a lot of personal problems, my daughter's been ill. I've got financial problems and normally I would get off my backside and start doing something about [smoking]. (P8, never quitter, female, age 67)*

A final sub-topic of this key theme was participants' description of the seemingly rebelliousness of their character preventing them from growing up and taking on adult responsibilities:

*It's a psychological rebellion in me that I'm pissed off having to work so hard but it's the one bloody thing in my life that I can rebel against cos I'm such an organised, orderly, disciplined person so there's something belligerent inside me that's saying 'go on, have a cigarette'. (P5, unsuccessful quitter, female, age 45)*

### VI.iii.ii.iv Negative effects of smoking

Throughout interviews, numerous references were made to the negative effects of smoking, which were either directly or indirectly acknowledged as well as denied by participants. For instance, some participants appeared to derogate the link between smoking and health risks:

*I still think that it's not proven. I think it's to do with people's low metabolism which has never been touched on. I think that some people can smoke and it has no effect on them, virtually none. (P15, unsuccessful quitter, male, age 74)*

Others down-played their own susceptibility to diseases:

*I'm sure there's some [effect]... like my lungs aren't going to be as happy as they were but I don't expect to get any long term health risks to be honest. (P19, never quitter, female, age 29)*

This is contrasted by interviewees, who accepted both the health risks of smoking as well as their own vulnerability to succumb to smoking-related diseases:

*As I was stopping smoking I realized that it was seriously damaging my health. (P3, successful quitter, male, age 39)*

Participants' responses also revealed a divergent attitude towards another negative effect of smoking – its addictive nature. Despite acknowledging that smoking can be addictive, many interviewees also maintained that they were not addicted:

*I'm not that sort of person that has to have cigarettes on me the whole time, in my bag or in my pocket. I'm not one of those people that wake up in the morning and have to have a cigarette.* (P12, unsuccessful quitter, female, age 34)

Moreover, participants not only down-played addiction but also negatively appraised quitting aids:

*I don't like the fact of patches or anything to be honest. I think you should do it yourself.* (P8, never quitter, female, age 67)

However, again there were also participants that acknowledged both their addiction to nicotine and thus the associated need for quitting medication to aid smoking cessation:

*No, it's the addiction to nicotine isn't it, the physical cravings that your body gets [...] I wouldn't have been able to do it without that [patches]. I had every faith in that working with me.* (P16, successful quitter, female, age 33)

### VI.iii.ii.v Triggers for quitting

Participants discussed a range of triggers that had motivated or could motivate them to stop smoking. Some triggers were associated with environmental factors and life-style changes:

*At the moment [quitting] is on my mind quite a lot, because as I say, I've got this marathon coming up that I need to start seriously training for, probably the week after next, probably 16 weeks training which is huge. That's shouldn't be a reason, that I'm doing a marathon but that will be a good spur to make me do it so I'm thinking about it quite a lot.* (P7, unsuccessful quitter, male, age 37)

But participants also mentioned inner conviction and motivation as a trigger for quitting:

*[I stopped] because I wanted to.* (P11, successful quitter, female, age 34)

Health was clearly recognised as a motivating factor for considering smoking cessation and was listed by a number of participants as the main trigger for quit attempts:

*If I suffered some serious health problems I would think that that is the time to stop.* (P18, never quitter, male, age 37)



### VI.iii.ii.vi Process of quitting

Smoking cessation itself was perceived by many as a hard process demanding a lot of commitment:

*No, it was not easy at all [...] I just got these enormous cravings that were quite short lived. Almost orgasmic cravings, really strong earth shattering things. (P3, successful quitter, male, age 39)*

By contrast, others felt that quitting was rather easy and nothing to be afraid of:

*I really thought that the third time would be even harder but it wasn't. It was much easier. (P11, successful quitter, female, age 34)*

Interestingly, a number of participants said that they enjoyed the challenge of quitting and that the social comparison with other people who have quit/are quitting motivated them even more to succeed in their attempt:

*But I did like the fact that I was asked, watching people saying: 'No I haven't smoked for a whole week' and I was thinking 'Well, if you can do it, I can do it'. (P2, unsuccessful quitter, female, age 62)*

### VI.iii.ii.vii Smoking and identity

A last key theme that emerged from the data relates to changes in participants' view of their own smoking, and smoking in general, as well as associated transitions in life-style. An indication of such change was the active dislike of oneself as a smoker:

*Smoking in general, I really hate it, I hate what I'm doing, I hate smoking around people, I hate inflicting diseases on people. I really hate doing it. (P5, unsuccessful quitter, female, age 45)*

as well as of other people smoking :

*Well, I found it really repulsive what she was doing and also it was completely inappropriate. You weren't allowed to smoke in that room. (P16, successful quitter, female, age 33)*

Many participants reported a change in their awareness of smoking, and noticing a shift in public opinion towards stigmatisation of smokers:

*I'll stand on her doorstep if I want a cigarette and I hate it when the neighbours come up. Think I'm awful because I smoke and I look down on people that come out of offices and stand there puffing away. (P8, never quitter, female, age 67)*

Interviewees said that they consequently felt ashamed of their smoking and therefore altered their life-style:

*I would never want to smoke walking down the street [...] it was a gradual process over many years, I started banning smoking from certain rooms in the house. So gradually, probably from outside. It hasn't suddenly become unsocial, it's been a gradual process.* (P9, unsuccessful quitter, female, age 66)

Indeed, many of the participants dissociated themselves from their current or former smoking (and thus their smoking identity) and expressed regret at ever having started:

*I don't see the point, I don't see the sense in doing it [smoking] anymore.* (P11, successful quitter, female, age 34)

*If I'd know how hard it was to quit I never would have started in the first place.* (P12, unsuccessful quitter, female, age 34)

Yet, as pointed out earlier, others were not unhappy about ever having started to smoke and felt that they had not substantially changed in terms of their identity or attitude towards smoking:

*I'm the same person but I don't smoke anymore.* (P3, successful quitter, male, age 39)

### **VI.iii.iii Progress towards smoking cessation I: Differences in self-accounts of people who have never or ever attempted to quit**

Self-accounts were very varied – both between and within groups. However, there were some indications that people who had never attempted to quit shared some views that were rarely expressed by people who had attempted to stop smoking. More specifically, when talking about their initiation into smoking, never quitters more readily provided reasons for starting to smoke that were not environmental but rather were intrinsically motivated such as curiosity, and wanting to know “what all the fuss was about”. Perhaps not surprisingly, never quitters talked a lot about their enjoyment of smoking and ascribed positive values to it and smokers in general:

*I just enjoy it, I enjoy smoking. [...] I've always met loads of interesting people on smoke breaks outside work and generally lots of my friends smoke so it's been a shared experience there.* (P21, never quitter, female, age 25)

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In terms of the more utilitarian aspect of smoking, while this was mentioned in all three groups, among people who had never attempted to quit, this was expressed in emotionally positive or neutral language, for instance:

*I enjoy taking five minutes away from my work up to ten times a day and having a cigarette. (P21, never quitter, female, age 25)*

By contrast, people who had attempted to quit, especially those that had failed, described smoking in more down-beat, melancholic language:

*Cigarettes seem to be my only solace. (P5, unsuccessful quitter, female, age 45)*

*So there's an element of loneliness, there's an element of not being fulfilled. So sometimes my cigarettes fulfil me because I'm bored. (P2, unsuccessful quitter, female, age 62)*

Never quitters rather down-played their susceptibility to smoking-related diseases and did not acknowledge the smoking-disease risk link:

*I don't feel an everyday kind of effect on my health. I mean if I am going to play squash or something like that, I mean I am still doing quite fine. (P23, never quitter, male, age 27)*

Interestingly, never quitters also seemed to be less willing to acknowledge addiction as a reason for smoking and displayed a negative attitude towards cessation aids compared with smokers who had attempted to stop:

*I don't get huge, overpowering urges to smoke. I chose to, I don't feel 'oh I need to go for a cigarette'. [...] I would be really wary of taking something that would interfere with my brain chemicals. Or start messing around with that kind of stuff. (P22, never quitter, female, age 26)*

Although some never quitters had even tried quitting aids (to cut down), their views of NRT were by and large very negative:

*That's what I tried [...] and found them really horrible. I don't know if the dose was too high but they made me feel quite anxious. Maybe it wasn't that you don't get the same hit so it wasn't doing the trick. I didn't really like patches. (P19, never quitter, female, age 29)*

One last pertinent and distinguishing feature in the self-account of never quitters relates to triggers for quitting. Across groups, most participants cited extrinsic motivators for stopping as well as health reasons but in contrast to both successful and unsuccessful

quitters, never quitters did not mention any potential intrinsically driven motivators (such as wanting to stop for oneself). Rather, it appears that never quitters wanted to absolve responsibility for taking the first step towards quitting and have someone else materialise to make them stop:

*If someone came into my life and said 'look we're going to do this if you give up smoking' and if my life wasn't such a hard slog and there wasn't so much stress around me, maybe I could do it. (P8, never quitter, female, age 67)*

Some never quitters even referred to their (presumably unchangeable) personality characteristics as a reason for their smoking:

*Also I feel rebellious about it. Like I'm talking to some devil about it [...] I'm almost rebellious about it. It's like being a naughty child again but who am I beating? (P8, never quitter, female, age 67)*

There were some people in this group who did not fit the general description of never quitters as focusing on enjoyment of cigarettes, displaying a low awareness of smoking-related risks, downplaying addiction and hoping for someone else to make them quit. These participants showed the most obvious signs of dissociating themselves from smoking by expressing regret at having started smoking and unhappiness about their current smoking. This shift in attitude was also accompanied by a change in awareness of what smoking stands for - from something that carries essentially positive connotations to something that has become a burden. This indicates a potential transformation in never quitters towards considering smoking cessation:

*When I was smoking heavily it was quite enjoyable at the time, but it feels less enjoyable now, so the attitude has changed from it being something exciting to something necessary, something that I do because I think I have to. (P19, never quitter, female, age 29)*

**VI.iii.iv Progress towards smoking cessation II<sup>35</sup>: Differences in self-accounts of people who failed or succeeded in their quit attempt**

The most striking difference in the self-accounts of successful and unsuccessful quitters was the implicit and explicit effort of unsuccessful quitters (similar to never quitters) to shift responsibility and blame for their smoking to factors that were external to them:

*The patches worked but unfortunately I got a rash and I had to stop, I was itching like mad, all the time. (P15, unsuccessful quitter, male, age 74)*

*I had a car crash and I'm now wearing a soft collar and I had put on weight and that bothered me and I thought to myself right, I'll have a cigarette instead of food that was it. That was the substitute for my food because I'd put on weight and I was really fat, fatter. (P2, unsuccessful quitter, female, age 62)*

Linked with these attempts to externalise responsibility for smoking (and thus self-justify the behaviour) was the identification of immutable, intrinsic factors – namely personality and rebelliousness – as reasons for continued smoking (which was again also observed among never quitters):

*I've got to try all these bad things...I've got this urge to do naughty things. Even if it is damaging me, I've got this compulsion to do naughty things. (P14, unsuccessful quitter, female, age 44)*

This was virtually non-existent in self-accounts of successful quitters. In fact, only one ex-smoker referred to their “addictive personality” when explaining their previous smoking pattern. In contrast to never quitters, unsuccessful and successful quitters alike made frequent references to the negative health effects of smoking as well as to addiction; however, unsuccessful quitters like never quitters also discounted and downplayed their own susceptibility to these health effects:

*I was always quite a fit person and did a lot of sports, horse riding, a lot of walking, a lot of swimming and I didn't really notice any negative effects. (P12, unsuccessful quitter, female, age 34)*

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<sup>35</sup> The term progress, used both in this and the previous heading, is not meant to prejudge whether the change from smoking to non-smoking is successive or sudden, rather it is simply trying to capture the idea of change in status (smoker/non-smoker or never attempter/ever attempter)

This is very much opposed to the views expressed by successful quitters, most of whom readily acknowledged their own susceptibility to smoking-related diseases:

*Yes. I always felt it was [damaging]. When I used to smoke normal cigarettes I was definitely aware that I would get a cough and feel a bit chesty. (P16, successful quitter, female, age 33)*

While both successful and unsuccessful quitters agreed on the addictive properties of cigarettes, unsuccessful quitters like never quitters were somewhat more dubious about the need of cessation aids even though they would have been exposed to the rationale of using these at the Stop Smoking Services:

*The physical side is always the easy side of quitting. My attitude towards smoking is the psychological side, the psychological addiction is the difficult part to crack. (P7, unsuccessful quitter, male, age 37)*

Successful quitters were convinced that smoking cessation aids had been crucial for the success of their quit attempt and thus maintained a largely positive attitude towards them:

*Certainly there is absolutely no way I could have done it without going to the clinic or the NRT. (P6, successful quitter, male, age 50)*

What then triggered smokers to attempt to stop in the first place? It seems that unsuccessful quitters put more emphasis on extrinsic motivators such as stopping for their partner or for pecuniary reasons rather than on their intrinsic conviction to stop. On the contrary, successful quitters in this sample talked about the growing realisation that they wanted to stop for themselves:

*I did it for myself, I wanted to. No one had a gun to my head. (P1, successful quitter, female, age 55)*

However, as there were some successful quitters who did not express such intrinsic motivation to stop, there were also some unsuccessful quitters who did:

*It actually has to come from within you. (P9, unsuccessful quitter, female, age 66)*

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Although more prevalent in accounts of successful quitters, health reasons and specific health-related incidents were the most frequent instigators of quit attempts cited by both successful and unsuccessful quitters:

*I kept getting a sore throat, I think, and I thought it was because of smoking. [...] I was getting worried. (P14, unsuccessful quitter, female, age 44)*

*Finding out that I actually do have something that can be affected by smoking [Hepatitis C] did really give me that push. (P6, successful quitter, male, age 50)*

Failure or success of the quit attempt did not appear to make a difference to the appraisal of quit attempts as hard or easy; both successful and unsuccessful quitters recounted a certain wariness regarding quit attempts as well as prior confidence in their ability to quit. However, in particular quitters who had succeeded, experienced quitting to be a personal challenge and, as already mentioned, found the social comparison with others motivating:

*I enjoyed seeing people that were far worse smokers than me. I thought that was great and the other thing that I found, people that said they only smoke 5 a day, they were the ones that dropped out. They were the ones that didn't turn up the next week. But that made me feel better as well, more willing to give up, and I did like to see people to drop out because it made me feel stronger. (P3, successful quitter, male, age 39)*

In terms of changes in general attitude towards smoking and changes in life-style, there was ample evidence from interviews of successful as well as unsuccessful quitters that most smokers who had attempted to quit had gone through some sort of transition:

*If I ever want to quit, this is the time to do it. A lot of people leave it till their 40s or 50s to quit but I don't want to do that. I want to do it now. I want to quit before I'm 35 and never smoke again. I want it to be a pivotal change in my life, where I actually grow up and become an adult. I've been a big kid all my life, a bit of an idiot really. (P12, unsuccessful quitter, female, age 34)*

*When you're in a professional job and you want to be professional about it, to still feel like that rebellious teenager to sneak out for a crappy cigarette and making excuses to, say 'I'm going to photocopy this', you feel really like this is immature behaviour. I felt less comfortable with that. (P16, successful quitter, female, age 33)*

Perhaps, the ultimate transition in a smoker's career – as expressed by successful quitters – was the realisation that it is not anyone else's but one's own responsibility to

stop. In contrast to never quitters, who waited for a saviour to help them stop smoking, and in contrast to unsuccessful quitters, who blamed others for their inability to stop, successful quitters talked about their sheer determination to stop and the acceptance of the fact that the future of their smoking career lay in their own hands:

*At the end of the day it's the person that goes to the clinic, it's their responsibility [to stop].* (P6, successful quitter, male, age 50)

*I went through a divorce and stressful jobs, there was always an excuse but they are all excuses. You always had an excuse for them, its not boredom or stress or anything like that. It's just that people want to keep smoking.* (P1, successful quitter, female, age 55)

*This time I was determined I was going to do it.* (P11, successful quitter, female, age 34)

There was a clear sense of dissociation from smoking among both unsuccessful and successful quitters. Most unsuccessful quitters regretted having started in the first place, and felt ashamed about their smoking:

*I have a terrible time of feeling so guilty and cross with myself. I hate it now. I don't want to be a smoker now, I don't want that.* (P9, unsuccessful quitter, female, age 66)

This dissociation and shift in identity, however, was much more complete among successful quitters, so much so, that the smoking self were considered an entirely separate entity from the current self as a non-or ex-smoker:

*And now I can't believe that I ever smoked. Oh, I'm very happy [to have stopped].* (P3, successful quitter, male, age 39)

Moreover, several interviewees expressed a feeling of pity for continuing smokers, suggesting the intrinsic segmentation between their former and current identity:

*When I see other people smoking I sort of feel a bit sorry for them really and think, ah they're still hooked, I feel a bit of sympathy. I don't feel any envy 'oh I wish I could have a cigarette' or anything.* (P16, successful quitter, female, age 33)

But this shift in identity or self-perception was not apparent in all self-accounts; as shown in the previous section. Some successful quitters did not feel that they or their views had changed very much because of giving up.



**VI.iii.v Synthesis: Derived typology and model of progression towards cessation**

In order to synthesise data further, typologies of different characteristics were developed (Table VI.II); however, the typologies are necessarily approximate and can therefore not provide a perfect fit for everyone in terms of all the characteristics considered therein.

**Table VI.II: Typology of participants**

Typology (Participants)	Characteristics
Committed smoker (P20, P21, P22, P23)	Never attempted to quit; enjoys smoking; believes smoking is intrinsic to them; ignorance/denial of health effects and addiction; happy to smoke
Aware smoker (P8, P18, P19)	Never attempted to quit; enjoys smoking; aware of health effects and addiction; shifts responsibility for quitting; unhappy about smoking; regrets starting; wary of quitting
Forced attempter (P4, P7, P12, P14, P15)	Attempted to quit; enjoys smoking; extrinsic motivation to quit; aware of health effects and addiction; downplays health risk & addiction; shifts responsibility for quitting; happy to smoke
Struggling attempter (P2, P5, P9)	Attempted to quit; doesn't enjoy smoking; intrinsic motivation to quit; aware of health effects and addiction; downplays health risks; regrets starting; wary of quitting; shifts responsibility for quitting; unhappy to smoke
Pragmatic ex-smoker (P3, P6, P10, P17)	Succeeded in quit attempt; used to enjoy smoking; health-related/extrinsic motivation to quit; acceptance of addiction & health risk; quitting hard; no regrets having smoked; accepts responsibility for quitting; feels like same person as before
Committed non-smoker (P1, P11, P13, P16)	Succeeded in quit attempt; intrinsic motivation to quit; acceptance of addiction & health risk; quitting easy; regrets having started; accepts responsibility for quitting; feels like different person

The 'committed smoker' (participant P23 is taken as an example here) had never attempted to give up cigarettes and still very much enjoyed smoking. They considered cigarettes as integral to their life and, more so, as part of their personality:

*So that's just like, you know, I just feel like that's kind of naturally me. (P23, never quitter, male, age 27)*

This participant was in denial about health effects and the health-risk link and also showed a lack of awareness of addiction:

*I can't really say if I am physically addicted. (P23, never quitter, male, age 27)*

‘Committed smokers’ were happy about their current smoking and consequently saw no reason to regret having started smoking in the first place:

*I love smoking cigarettes. [...] So, I don't really regret it.* (P23, never quitter, male, age 27)

The ‘aware smoker’ (participant P18 functions as an example of this typology) had also never attempted to quit smoking and still enjoyed cigarettes but in contrast to ‘committed smokers’ was more aware of the health effects of smoking and of the possibility of addiction:

*[...] but it's just pure addiction.* (P18, never quitter, male, age 37)

This greater awareness meant that smokers were unhappy about their smoking and regretted having started. Consequently, there was a greater need to justify their behaviour, which explains why participant P18 expressed wariness when it came to considering quitting and shifted responsibility for smoking to external factors:

*A lot of people that I work with smoke and that propagates me to decide not to give up smoking.* (P18, never quitter, male, age 37)

Among smokers who had attempted to quit, it was possible to differentiate ‘forced’ from ‘struggling attempters’. The ‘forced attempters’ (participant P15 is an exemplar of this type of smoker) were quite similar to the ‘committed smoker’ with the exception that they displayed more awareness for the health consequences of smoking. However, this did not mean that they had actually accepted the health risks and their susceptibility to it:

*The CO thing, if you think about it and I'm driving 18 hours a day in London traffic, the amount of CO I'm getting is probably 5 times as much as what I'm getting from cigarettes anyway.* (P15, unsuccessful quitter, male, age 74)

Perhaps the most striking feature of the ‘forced quitter’ was that they had stopped primarily for extrinsic reasons and did not show any obvious signs of being internally motivated to quit:

*I stopped purely for my wife.* (P15, unsuccessful quitter, male, age 74)

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Similar to 'aware smokers', participant P15 was also shifting responsibility for the ongoing smoking but unlike 'aware smokers' was quite adamant that he was happy to smoke and did not regret having started:

*[I'm] happy that I smoke [...] I do enjoy it because it occupies me and makes me apparently relaxed. (P15, unsuccessful quitter, male, age 74)*

Quite the opposite was expressed by 'struggling attempters' such as participant P2, who were desperate to stop smoking and very unhappy about their failure to stop:

*Terribly, oh my goodness, terribly, terribly, terribly, 100 %. Yes, I regret having started smoking [...]. In the year that I did stop smoking I felt much, much healthier. I felt fresher, more alive. I felt much, much healthier. I felt really good. (P2, unsuccessful quitter, female, age 62)*

In contrast to the 'forced quitter', this participant accepted the health risks associated with smoking but again attempted to shift the responsibility for their smoking to external sources:

*[On a friend that has managed to quit] But then she's got a son and a daughter and they've got children and she's very busy, and she's a lovely person and she has lots of nice friends and so for her family and the children, she's made a greater effort than I have (P2, unsuccessful quitter, female, age 62)*

The 'struggling quitter' did not enjoy smoking and was intrinsically motivated to quit:

*[I stopped] because I wanted to rather than then had to. (P2, unsuccessful quitter, female, age 62)*

However, despite the internal pressures, participant P2 was unable to stop and consequently acutely aware of how hard it was to kick the habit:

*[Quitting] really was difficult [...] I did not feel confident. I did not feel confident whatsoever. (P2, unsuccessful quitter, female, age 62)*

There were two types of successful quitters; the 'pragmatic ex-smoker' and the 'committed non-smoker'. The 'pragmatic ex-smoker', as in the case of participant P17 presented here, was open about their previous enjoyment of cigarettes and did not regret having started smoking:

*It actually meant relaxation [...] I don't really regret [starting] as such. (P17, successful quitter, male, age 55)*

This participant accepted the negative consequences of smoking and their susceptibility to it. Indeed, signs signifying deterioration in health status were the overriding factor that initiated smoking cessation:

*There were a number of key factors that made me come to that decision. I don't think I can say that I suddenly decided to give it up. Although having said that, I had had a blood pressure check and it was a bit high and I thought well, ... I know the associations between smoking and cardiovascular problems. (P17, successful quitter, male, age 55)*

'Pragmatic ex-smokers' acknowledged how hard it was to stop smoking and were grateful for the support they had received from quitting aids. Moreover, 'pragmatic ex-smokers', in contrast to 'struggling attempters', also accepted responsibility for their own behaviour, the need to quit and described changes in their life-style associated with quitting:

*I did notice that one change was that I found it very offensive to be in smoking places, so yes I did start to avoid going to pubs, which I didn't do that much before but I did make a conscious effort to not go to those places. (P17, successful quitter, male, age 55)*

However, they felt that they had not changed otherwise and had stayed very much the same as before - only that they were not smoking anymore.

*I don't feel a changed person. (P17, successful quitter, male, age 55)*

In comparison to 'pragmatic ex-smokers', 'committed non-smokers' felt that stopping smoking was accompanied not only by an external but also internal change and participant P16 is a good example of this type of smoker:

*I'm a different person, I've just grown up I think, that's the difference. (P16, successful quitter, female, age 33)*

This participant, while also acknowledging health problems as a reason for quitting, nonetheless more strongly emphasised intrinsic reasons for stopping smoking:

*[I stopped] because I wanted to. I felt the time was right. (P16, successful quitter, female, age 33)*

Like 'pragmatic ex-smokers', 'committed non-smokers' accepted responsibility for their smoking acknowledging that in the end it came down to oneself to quit:

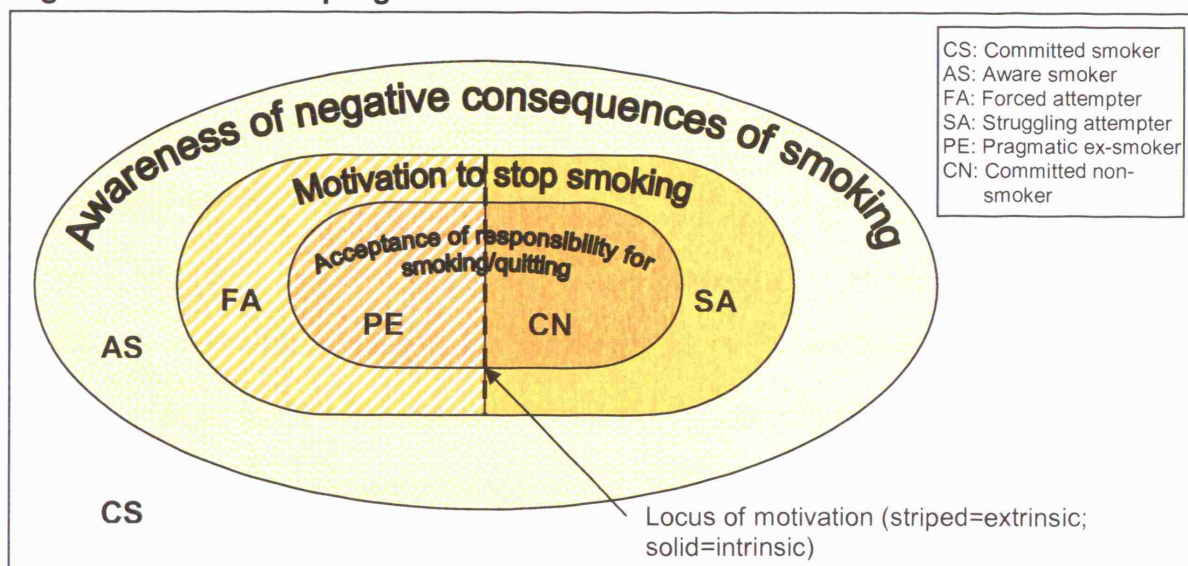
*I don't think you can force someone to give up if they don't want to give up, it's their decision. (P16, successful quitter, female, age 33)*

Unlike 'pragmatic smokers', however, participant P16 regretted having started in the first place and found their quit attempt easier:

*I think I was just lucky; I just had an easy ride really. (P16, successful quitter, female, age 33)*

As a last step in the synthesis, the different typologies that could be derived from the data were used to develop a possible parsimonious model. As the typologies appeared to describe a succession of changes in people's self-accounts, the resultant model is one that captures this progression towards smoking cessation (see Figure VI.II). It attempts to coherently classify the various types of smokers and ex-smokers in this study using the smallest number of differentiating factors.

**Figure VI.II Model of progression towards cessation**



As there were no striking socio-demographic patterns emerging from typologies (with the possible exception of age<sup>36</sup>), these did not feature in the model. From the descriptive

<sup>36</sup> Forced attempters were somewhat older than struggling attempters and pragmatic ex-smokers older than committed non-smokers. The former may be due to the fact that the external (such as financial) and health pressures to stop typically cited as reason for quitting by forced attempters become more prevalent as smokers grow older. The latter may also be related to this. In addition, it may be easier for younger

account it is clear that 'committed smokers' were, not surprisingly, least aware and accepting of the negative effects of smoking. In this model it is postulated that smokers, however, do become more strongly aware of these effects, as exemplified by the 'aware smoker', even though they may not necessarily admit susceptibility to the effects. Yet, without sufficient internal or external pressure (or intrinsic/extrinsic motivation<sup>37</sup>), 'aware smokers' will not attempt to quit.

'Forced attempters' are aware of - but don't accept their susceptibility to - the negative effects of smoking. However, being extrinsically motivated to stop at least results in a quit attempt, albeit unsuccessful. 'Struggling attempters' are both aware of the negative health effects and more accepting of their susceptibility to it. Consequently, they feel intrinsically motivated to stop and thus attempt to quit, even if this is unsuccessful. The model postulates that both types of attempters fail in part because they have not internalised the responsibility for their action. Rather, they see it as someone else's task to make them stop. It is, however, acceptance of one's own responsibility to change the behaviour and the resolve to stick with it, which differentiates successful from unsuccessful quitters in their self-accounts.

While it is impossible to tell from the data if this is a *post hoc* rationalisation, neither 'pragmatic ex-smokers' nor 'committed non-smokers' deny their own susceptibility to the effects of smoking but report having finally accepted that it is only they themselves and nobody else who can ensure that they succeed. Thus the model proposes that it is the combination of having awareness of and accepting the negative health effects of

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smokers to completely renounce and change their smoking identity to that of a non-smoker since smoking may not have been as ensconced in their lives as in that of older smokers who quit.

<sup>37</sup> In this model, it is postulated that people rationalise and describe their motivation to change behaviour as either linked to external or internal reasons. This, however, is not to say that motivation is external to the person (it works through the internal motivational system) but that it can be instigated by external sources.

smoking, extrinsic (as in the case of 'pragmatic ex-smokers') or intrinsic motivation (as in the case of 'committed non-smokers') to stop smoking and, crucially, internalised determination and acceptance of the need to take responsibility for stopping smoking, which yields a successful quit attempt.

It is beyond the remit of this chapter to elaborate on either the various phases of transitions between these different levels or the influences on the transition, but it is clearly conceivable that smokers may jump phases or move back and forth from one to another level, being influenced by a variety of factors including nicotine dependence, socio-economic status and availability of (behavioural or pharmaceutical) help. However, *ceteris paribus*, this simple model argues that a smoker's behaviour (both attempting to quit and succeeding in the quit attempt) is ultimately determined by the interplay of awareness, motivation and an ensuing acceptance of taking responsibility for their own actions.

### **VI.iii.vi Service users' views of NHS Stop Smoking Service (SSS)**

Overall, responses of service users were very positive and this applied to both people who had failed as well as succeeded in their quit attempt:

*I don't know how they did it but they stopped me smoking. So I praise all of them there.* (P2, unsuccessful quitter, female, age 62)

*When I phoned I found them very helpful, good information. I joined the group, the ladies there were very nice and understanding and straight to the facts. [I would recommend it to a friend] most definitely.* (P4, unsuccessful quitter, female, age 43)

*I think they do an awfully good job.* (P9, unsuccessful quitter, female, age 66)

*I think it's great, it was the best thing that's happened.* (P6, successful quitter, male, age 50)

*I think its fabulous. I'm really pleased I went along.* (P10, successful quitter, female, age 42)

*All of it, it was absolutely marvellous, it was really, really good.* (P16, successful quitter, female, age 33)

More specifically, services users praised the positive and open atmosphere:

*It was that kind of atmosphere that if you wanted to know more, you could ask. It was a very open forum. They explained everything in detail and if there were things that you weren't sure about, you could ask and it was explained. (P1, successful quitter, female, age 55)*

*I thought the attention and the consideration shown and attention individually and the way it was operated was very professional. (P17, successful quitter, male, age 55)*

as well as flexibility of the Stop Smoking Services:

*You could phone them up to several weeks later or go back to an individual session two or three months after, so there was a follow up, which was good. (P7, unsuccessful quitter, male, age 37)*

*And they were quite good, if we didn't make it they said don't worry, you can do another course. It other words they weren't shutting the door on you. (P9, unsuccessful quitter, female, age 66)*

However, not everybody was quite so positive. Perhaps unsurprising, negative comments were confined to self-accounts of smokers who had either never attempted to stop smoking or who had failed to do so. Among unsuccessful quitters, the negative view of the SSS stemmed either from personal antipathy:

*We were like guinea pigs for [the group leader] and she didn't have any other interest in us. (P5, unsuccessful quitter, female, age 45)*

or the content of what was offered at the SSS:

*I did find the service quite basic in its approach. (P7, unsuccessful quitter, male, age 37)*

Interestingly, the negative comments that were most prevalent among never quitters likened the SSS to Alcoholics Anonymous:

*[...] to turn up like Alcoholics Anonymous, I don't think its for me really. (P18, never quitter, male, age 37)*

*Is it like the Alcoholics Anonymous meetings on TV? (P21, never quitter, female, age 25)*

*But you get the impression it's gonna be a bit like Alcoholics Anonymous. (P22, never quitter, female, age 26)*



## Chapter VI: Study 2 - Qualitative enquiry of smoking cessation

Another related, divisive, and recurring issue in interviews was participants' appraisal of the use of groups in the SSS. Most successful quitters expressed very positive views regarding the utilisation of groups in the SSS. Successful quitters, for instance, commented on how helpful it was to share their experience with others:

[It was very helpful -] *the buddy system and hearing about peoples' experiences.* (P1, successful quitter, female, age 55)

*It really works that group therapy. Is it exactly as you imagine; as in a Woody Allen film, you do sit around and talk about your smoking problems.* (P3, successful quitter, male, age 39)

*It was really good, it made you feel really good that it wasn't just you that was giving up. You were a part of this group and all of you were working towards this amazing achievement that you could share.* (P16, successful quitter, female, age 33)

Successful quitters also highlighted that they felt it was important and useful to hear stories of other smokers so as to normalise their own experiences and to overcome a sensation of solitude with regard to the emotional and physiological changes they were going through:

*I felt the sort of talking about cravings and things like that, I found that very helpful because you realise you are not alone.* (P6, successful quitter, male, age 50)

[...] *helpful was the fact that I had to listen to everybody in turn and it made me realize that I was in the same boat.* (P17, successful quitter, male, age 55)

Both smokers who had either failed or succeeded in their quit attempts also remarked on the sense of shared support and commitment they developed as being part of a group:

*I thought the group overall was very good, very informative, very supportive, we exchanged numbers with people that we could contact.* (P4, unsuccessful quitter, female, age 43)

*But with this group we'd all made this commitment together. I didn't want to be the one that let other down.* (P9, unsuccessful quitter, female, age 66)

*But actually for me, made it much easier, because I wasn't just doing it for me, I was doing it for everyone else in that room as well. If I had failed, it wouldn't have just been me that failed, it would have been the whole group.* (P11, successful quitter, female, age 34)

A negative view of groups was mostly confined to never quitters and unsuccessful quitters and either related to personality characteristics or preference:

*I'm not good in group situations like that. (P21, never quitter, female, age 25)*

*And I didn't really respond.... I am not the sort of person, who responds to the 'open your heart up to a whole load of strangers', so I didn't actually find it very useful in terms of giving up as a group. (P14, unsuccessful quitter, female, age 44)*

or to anticipated or experienced practical problems:

*In a group situation you get the impression you might be sat there for 50 minutes bored out of your brains. (P22, never quitter, female, age 26)*

*The group, quite honestly, was a waste of time because there were 60 people in the group and by the time you went round, it was time to go home. (P15, unsuccessful quitter, male, age 74)*

Participants' suggestions for improvement of the SSS were connected to these negative comments. These suggestions concerned either the content of the SSS programme, structure and access to the SSS or flexibility in the interventive approach taken by the SSS. Most common were proposals regarding access to the SSS since a number of never and unsuccessful quitters felt that current availability of smoking cessation clinics in terms of location and time prevented them from attending the service:

*[SSS] is a bit inflexible, which is difficult if you're working and so on. (P19, never quitter, female, age 29)*

*I would also like if there was more of a variety of times. (P4, unsuccessful quitter, female, age 43)*

*I suppose more choice for people... what suited them. So, much more local groups because there's only that one in the whole area. (P14, unsuccessful quitter, female, age 44)*

Some participants liked the idea of an opportunistic service that could be attended whenever there was a need:

*But something that I could go to when I really felt like I was gonna have a cigarette and I could just go and complain to somebody. (P22, never quitter, female, age 26)*

## Chapter VI: Study 2 - Qualitative enquiry of smoking cessation

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*So I would probably design it so that there was a group session once a week with every other day drop in session where you could go in if you needed that support. (P13, successful quitter, female, age 58)*

Relating back to the dislike of groups, unsuccessful quitters but also those who had succeeded, felt a need for reducing the size of groups:

*Maybe they [groups] should be a bit smaller. Just too large to get any sense of intervention. (P7, unsuccessful quitter, male, age 37)*

*[There] could have been smaller groups. (P13, successful quitter, female, age 58)*

In terms of the content of the programme of the SSS, there was not much agreement between various participants. While some thought that the depth of information presented was just right, others wanted additional information and a more 'psychological approach':

*There could have been more slide shows. I think when everybody got to the group they expected to see all these slide shows about how smoking was damaging their lungs, terrible pictures, disgusting things. I think everybody was quit disappointed that we weren't going to see that. (P12, unsuccessful quitter, female, age 34)*

*I think a lot of the psychological aspects could be used a bit more to get people to realise that they are not giving anything up because it isn't, you're not giving anything up, you're just stopping doing something that is really unpleasant at the end of the day. (P6, successful quitter, male, age 50)*

Especially unsuccessful quitters also felt that the SSS needed to cover more specific skills:

*[I wanted more info on] dealing with the eating habits. (P2, unsuccessful quitter, female, age 62)*

*How to deal with a relapse... Just a little touch on relapse prevention but I don't think it was ever mentioned. (P7, unsuccessful quitter, male, age 37)*

The last area of improvement mentioned by a couple of participants related to the lack of diversity in SSS or rather the stringency of the approach taken to delivering the services.

In particular, it was felt that the SSS should more readily acknowledge that there are different methods and ways for giving up:

*[...] maybe promote the idea of giving up smoking and say these are the different methods you can have, counselling, or patches but I wouldn't promote just one way to stop. (P21, never quitter, female, age 25)*

*I think that you instinctively know when you can get away with it, and if you can't get away with it, you have two halves [of nicotine gum]. I think you can gauge it yourself and they don't really give you credit for that, they tend to think that everybody is the same. (P6, successful quitter, male, age 50)*

In general, however, the view of the services was positive and this was underlined by the fact that many of those who had failed were happy with the services and unable to suggest further improvements.

### **VI.iii.vii Views of current and ex-smokers on smoking cessation interventions involving biomarker feedback**

In the latter part of the interview participants were asked their opinion about the use of biomarker feedback in smoking cessation interventions. The concept of biological markers of smoking-related harm, risk or exposure was explained to participants and their comments invited. In general, participants gave a positive response to the suggested use of biomarker feedback in interventions. In fact, even before the topic of biomarker feedback was touched upon in the interview, a fair number of participants had already commented on the effect of being provided with carbon-monoxide readings (a biomarker of exposure and risk) at the SSS and how useful they thought it was:

*[It's] helpful to have that carbon monoxide test. One week it was showing 25 and then next week it was blowing 4 or whatever. (P7, unsuccessful quitter, male, age 37)*

*I had a high reading and I was really horrified [...]. (P9, unsuccessful quitter, female, age 66)*

*The testing [was particularly useful], it went down to virtually zero. (P15, unsuccessful quitter, male, age 74)*

*I really liked the CO tester, it was very vivid [...] The second reading gave me a shock. (P3, successful quitter, male, age 39)*

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*But even so with the numbers on the carbon monoxide was enough to scare me. (P16, successful quitter, female, age 33)*

Most participants, irrespective of whether they had attempted to stop or not, thought that giving biomarkers feedback would encourage them to stop smoking as it personalised the threat that smoking represented:

*I think that's pretty good, psychologically. Because you think that it's happening to all the others, but it ain't going to happen to you. If you see something that is happening, I think that is something that would be a bit of a boost, that's my opinion. [...] It would scare me off and it would make me do something. It would give me the kick up the backside to put it crudely. (P8, never quitter, female, age 67)*

*If you have the full information it would definitely worry you and to know that you're at risk. The will to give up smoking must surely get stronger. (P18, never quitter, male, age 37)*

*I would do something about it. Because I enjoy life, very much and it would really put me off [...]. (P2, unsuccessful quitter, female, age 62)*

*So it could be a good scare tactic basically. A good confronting factor [...] the signs [of damage] would definitely spur me into action. (P7, unsuccessful quitter, male, age 37)*

*That is great. It certainly would have helped me. In the past, this time I had a reason, but certainly in the past it would have given me more of a push. (P6, successful quitter, male, age 50)*

*It would have made me more determined and I probably would have given up many years ago. (P11, successful quitter, female, age 34)*

Indeed, some participants explicitly mentioned the motivating impact of receiving blood pressure readings on their motivation to stop:

*I'd been going to the doctors to get my blood pressure checked and it was really high. I had to get onto a different contraceptive pill and that was another thing that made me want to stop as well. (P16, successful quitter, female, age 33)*

However, a few interviewees were also sceptical about the impact of biomarker feedback. With regard to older smokers, some participants thought that these may not be moved to stop smoking by any intervention offered:

*Lots of elderly people that smoke that are going around with their walking stick and they won't give up but you know, if they are shown that they have damaged themselves, the really old ones, they aren't going to care anymore. (P1, successful quitter, female, age 55)*

*I don't know if it would have helped my father for instance, who in fact was developing all these symptoms and died from it eventually. I think he may have thought 'well I'm going to die anyway, I'll just carry on'. I think certainly with older smokers they think I can't live forever. (P10, successful quitter, female, age 42)*

Another concern, on the one hand, was that smokers may be reassured to continue smoking if no harm or risk was found:

*I mean it could easily be a backlash. Look at me - fully healthy. I think that could be a problem. (P23, never quitter, male, age 27)*

*Well, if it all looked fine, I'd probably think ah, that's alright then and carry on smoking. (P14, unsuccessful quitter, female, age 44)*

Yet, on the other hand, participants worried about biomarker feedback scaring smokers too much without offering sufficient support:

*[If you] put too much pressure on giving up smoking and then if they've seen it and decide to give up smoking and haven't succeeded the worry must be immense. (P18, never quitter, male, age 37)*

*I think there is a risk of scaring people too much and making them think that something bad is going to happen. (P19, never quitter, female, age 29)*

*I suppose it might scare some people. (P9, unsuccessful quitter, female, age 66)*

Therefore, some participants felt that smokers may avoid interventions that involve biomarker feedback outright:

*A lot of people [...] won't want to see what's happening, scared of those results. And obviously you can't make them, can't make it compulsory. (P11, successful quitter, female, age 34)*

*It might have frightened the hell out of me, so I may not have wanted that done. (P17, successful quitter, male, age 55)*

How then can interventions that use biomarker feedback be improved? Study participants suggested three ways to overcome some of the perceived problems. First, to avoid scaring smokers unduly, they proposed proper debriefing after interventions with biomarker feedback to ensure smokers are aware of the implications of the results:

*I think if it was me and something was found, I would want some de-briefing or more information. Ask questions about the specific implications of that. (P19, never quitter, female, age 29)*

*There would have to be a process of discussion beforehand and afterwards and what was then going on in the rest of your body, so that people could answer if they have never really considered what's going on in their own body, there'd need to be somebody there who could do that. (P22, never quitter, female, age 26)*

Second, in order to motivate smokers who would otherwise not respond to the intervention, it would be helpful to be able to demonstrate a change for the better.

*So probably doing [the intervention] at 30 and doing it at 40 again of the same person and show the differences there, that would help convince me much more. So both the reference and the effect is kind of your own. (P23, never quitter, male, age 27)*

*If there was improvement [in biomarker] it would be great because then you could show people the improvement. (P12, unsuccessful quitter, female, age 34)*

Third and last, it was suggested to include both some sort of associated behavioural experiment:

*I would probably make them do something, which they are very confident they could do ten years ago or something like that and they realise that they can't do it, not running a half-marathon but something physical. (P23, never quitter, male, age 27)*

and to highlight the possibility of future damage to avoid reassuring smokers to continue smoking and to strengthen the impact of this kind of intervention:

*You could show some sort of simulation of [the damage] happening; how it progresses. (P14, unsuccessful quitter, female, age 44)*

It is interesting to note that proposals for improvement were only offered by current not ex-smokers. Altogether then, while participants saw a number of possible problems with this type of intervention, it was considered both potentially helpful and acceptable, given appropriate precautions.

### **VI.iv Discussion**

This study was designed to investigate smoking cessation in the UK from a qualitative perspective in order to inform current and future interventions by focusing on the self-

accounts of smokers who had either failed or succeeded in their quit attempt and those who had never attempted to stop.

### **VI.iv.i Findings in relation to existing literature**

#### **VI.iv.i.i Process of smoking cessation**

This study expanded on existing qualitative literature by both revealing novel insights into the process of smoking cessation, and by confirming previous findings in a new setting, relevant to England. Participants' description of their smoking career started with the early initiation into smoking owing to peer pressure and a desire to fit in, which has been reported in other qualitative studies (e.g. Thompson, Thompson, Thompson, Fredrickson *et al.*, 2003; Wiltshire, Bancroft, Parry, & Amos, 2003; White, Bush *et al.*, 2006). However, in this study additional internal triggers of smoking like curiosity were also identified.

The enjoyment that smokers gain from cigarettes is often reported (Bott, Cobb, Scheibmeir, & O'Connell, 1997; Lai & Lau, 2005; Petek, Rotar, Svab, & Lolic, 2006) as are the utilitarian aspects of smoking, e.g. stress relief (Balch, 1998; Seguire & Chalmers, 2000; Vuckovic, Polen, & Hollis, 2003). Another finding, which also resonates with the literature, is the extreme emotional attachment to cigarettes that was expressed by some participants (e.g. the cigarette as a friend), specifically by older and heavier smokers (Bott, Cobb *et al.*, 1997; Thompson, Thompson *et al.*, 2003).

The other side of the coin, including the negative health effects of smoking, was often ignored or down-played in the accounts of smokers and this has also been observed in other qualitative studies, in which participants discounted their smoking as not as serious as other behaviours (Balch, 1998), displayed optimistic bias (Foraker, Patten, Lopez, Croghan *et al.*, 2005; Lai & Lau, 2005; Petek, Rotar *et al.*, 2006) or even argued



that smoking-related health risks were subjectively constructed (McKie, Laurier, Taylor, & Lennox, 2003). Moreover, previous studies have shown that smokers may also passively accept this risk or discount future risks (Kulwicki & Rice, 2003; McKie, Laurier *et al.*, 2003; Petek, Rotar *et al.*, 2006), something which in the current study is encapsulated by the typology of the 'aware smoker'.

Addiction to cigarettes has also been downplayed or denied by smokers in previous studies (Kishchuk, Tremblay, Lapierre, Heneman *et al.*, 2004; Lai & Lau, 2005; Amos, Wiltshire, Haw, & McNeill, 2006) and in the current study was most prevalent among 'committed smokers' who had not attempted to quit. Indeed, qualitative research suggests that an awareness of addiction develops once smokers have attempted to quit (Puskar, 1995; Petek, Rotar *et al.*, 2006; Amos, Wiltshire *et al.*, 2006) and this was corroborated by the differences in awareness displayed by never quitters and unsuccessful or successful quitters. Associated with the down-playing of the addictive aspect of smoking as well as with previous quit failures was the negative appraisal of quitting aids, which has been reported in earlier studies (Wiltshire, Bancroft *et al.*, 2003; Kishchuk, Tremblay *et al.*, 2004; Foraker, Patten *et al.*, 2005; Lai & Lau, 2005; White, Bush *et al.*, 2006; Amos, Wiltshire *et al.*, 2006)

The general finding that the causal schema of current smokers involved a derogation of susceptibility to the negative effects of smoking can be interpreted within the context of cognitive dissonance theory (Festinger, 1957). Festinger suggests that cognitions, which are relevant to each other, such as the perception of the consequences of a behaviour and the attitude towards the behaviour, can be either consonant ("smoking causes health problems, I do not want health problems, therefore I do not smoke" or "smoking does not cause health problems, and I enjoy smoking, therefore I smoke) or dissonant

(“smoking causes health problems, I do not want health problems, but I smoke”). For smokers that are aware of the negative effects, this awareness creates these dissonant cognitions. In order to reduce the resultant dissonance, which is perceived as uncomfortable, participants would have been motivated to engage in one of two strategies: to remove the dissonant cognition (stop smoking) or to alter the dissonant cognitions (either “smoking does not cause health problems” or “smoking may cause health problems but not for me” or even “I don’t mind getting health problems”). This may explain why both unsuccessful quitters and the ‘aware smoker’ were keen to deny the negative effects of smoking. In contrast, both ex-smokers and the ‘committed smoker’ have consonant cognitions (albeit in the opposite direction) and thus are not as motivated to down-play smoking-related risks.

A range of factors that triggered quit attempts were present in self-accounts and, in agreement with the literature (e.g. Balch, 1998; Vuckovic, Polen *et al.*, 2003; White, Bush *et al.*, 2006), health concerns were most prominent among these. As in other studies (Foraker, Patten *et al.*, 2005), the motivating influence of family was also described in this study but in contrast to previous research (White, Bush *et al.*, 2006; Amos, Wiltshire *et al.*, 2006), quit advice from health professionals was not explicitly mentioned, and perhaps this was an artefact of the study sample. Most participants (but not all) who had attempted to stop acknowledged that smoking cessation was a tough process, a ubiquitous finding in the qualitative literature on cessation (e.g. Bott, Cobb *et al.*, 1997; Ahijevych, Kuun, Christman, Wood *et al.*, 2003). However, the study also revealed differences in the appraisal of the quit attempt. Ex-smokers in particular described their quit attempt as a challenge and enjoyed the competitive aspect of giving up.

This finding has relevance within the framework of social comparison theory, which postulates that people look to their environment and other people in order to both evaluate and enhance some part of the self (Suls, Martin, & Wheeler, 2002). In particular, downward social comparison seemed to be relevant to many ex-smokers' descriptions of their own quit attempt as well as to their appraisal of others. Seeing fellow smokers fail to quit motivated some ex-smokers not to become part of this group and to succeed in their attempt. Likewise, seeing people who were appraised as less able than themselves succeed in giving up also motivated former smokers to stop.

Those smokers that had not stopped smoking, either because they had not tried or because they had failed in the attempt, were ready to supply a list of reasons why they were still smoking. Shifting blame to others and absolving oneself from responsibility has been reported in a number of earlier studies. Smokers point the finger to friends and family (e.g. Ahijevych, Kuun *et al.*, 2003; Kulwicki & Rice, 2003; Panday, Reddy, & Bergstrom, 2003; Foraker, Patten *et al.*, 2005); to their economic circumstances (Wiltshire, Bancroft *et al.*, 2003); to the health services and society in general (e.g. Rajamaki, Katajavuori, Jarvinen, Hakuli *et al.*, 2002; Lai & Lau, 2005) as well as to their addictive personality (Thompson, Thompson *et al.*, 2003). However, another aspect of this denial of responsibility that has not been highlighted in the literature thus far, and to which participants in this study made frequent reference, was the self-perception as a rebel. A number of smokers appeared to construct this identity in their self-descriptions, which was used to explain their continued smoking, i.e. the desire to not conform to society and to not give in to the societal pressure to quit because of their rebellious nature.

This extrinsic social pressure to stop that was anticipated by the rebellious smokers was also cited as a reason for quitting by some but not all unsuccessful quitters, especially the 'forced attempters'. 'Struggling smokers' in comparison also mentioned intrinsic motivation as a reason for quitting, which mirrors findings from other studies, which imply that motivation to stop has to come from within (e.g. see Rajamaki, Katajavuori *et al.*, 2002; Vuckovic, Polen *et al.*, 2003; Foraker, Patten *et al.*, 2005). However, according to the ex-smokers in this study, one has to go beyond motivation in order to succeed and the next step in the progression towards cessation is to accept responsibility for one's own actions; something which has been described as a process of personal growth elsewhere in the qualitative literature on smoking cessation (Puskar, 1995).

This process is perhaps best understood from the vantage point of identity shift theory, which proposes that the distress, conflict and dissonance that result from continuing a certain behaviour cause a succession of small changes (or steps) both in attitude and behaviour that culminate in an identity shift (Kearney & O'Sullivan, 2003). In this, as in other qualitative studies (e.g. Seguire & Chalmers, 2000; Petek, Rotar *et al.*, 2006; Amos, Wiltshire *et al.*, 2006) some smokers ('committed smokers') will see their smoking as very much part of who they are (hence rebelliousness) while some (e.g. 'struggling quitters') will openly express their dislike of others' as well as their own smoking; this growing negative attitude towards smoking is common in smokers' self-accounts (e.g. see Butler, Pill *et al.*, 1998; Seguire & Chalmers, 2000; Rajamaki, Katajavuori *et al.*, 2002).

The build-up of dissatisfaction gradually erodes the concept of the self as a smoker and leads to the adoption of a new identity – the 'committed non-smoker'. In the current as well as in a previous study (Vuckovic, Polen *et al.*, 2003), ex-smokers said that they

realised at some point that a change in life-style was required. Previous studies also suggest that stigma may be an important contributor to this process (Puskar, 1995; Wiltshire, Bancroft *et al.*, 2003). However, in addition, this study also elucidates a different pathway towards cessation, one which is not as closely tied to a change in identity but rather, as exemplified by the 'pragmatic ex-smokers', to a realisation of the necessity of quitting and the futility of shifting responsibility to others. This behaviour change thus appears less connected with internal changes than it is with extrinsic motivators and would, at least in part, explain the effectiveness of policy changes that primarily manipulate external factors such as increasing taxation on cigarettes or introducing smoking bans (e.g. see Aquilino & Lowe, 2004).

### **VI.iv.i.ii Views on Stop Smoking Services**

This is one of only a handful of studies, which has qualitatively investigated service users' views of smoking cessation clinics and the first that could be found to do so in England. Both successful and unsuccessful quitters expressed mixed views of group counselling; while some participants had found them very useful, others had disliked them. The divided stance towards group counselling has been previously reported with some studies finding that groups were positively appraised (Rajamaki, Katajavuori *et al.*, 2002) and others finding the opposite (Balch, 1998). Moreover, the stigma attached to the services (as being likened to Alcoholics Anonymous) has been reported before in a study of Scottish adolescents (Amos, Wiltshire *et al.*, 2006). A popular suggestion for how to improve the stop smoking services was to increase the accessibility to clinics and to introduce opportunistic services, both of which have also been suggested by participants in other qualitative studies (Ahijevych, Kuun *et al.*, 2003; Lai & Lau, 2005; Amos, Wiltshire *et al.*, 2006). However, in addition and connected with the ambivalent attitude towards group counselling, this study also highlighted users' dislike of

overcrowded group sessions in the SSS and the proposal to reduce the number of people per group.

Most participants in the present study thought that the services provided sufficient material and this confirms reports that smokers prefer to have only relevant and concise material provided in smoking interventions (Balch, 1998; Ahijevych, Kuun *et al.*, 2003). Another finding also reported in previous research is the dislike of a perceived rigid, top-down approach taken by quit services (Balch, 1998; Butler, Pill *et al.*, 1998; Ahijevych, Kuun *et al.*, 2003). However, the need for additional skills to be imparted in the quit clinics, which was expressed by participants in this study, has not been explicitly described in earlier studies (but see Vuckovic, Polen *et al.*, 2003). Interestingly, two themes often described in the literature did not feature prominently in the current study - the characteristics of the counsellor (e.g. Kishchuk, Tremblay *et al.*, 2004; Foraker, Patten *et al.*, 2005) and the need for an empathic, sympathetic approach to smokers in cessation interventions (e.g. Bott, Cobb *et al.*, 1997; Vuckovic, Polen *et al.*, 2003). Presumably, this may reflect participants' satisfaction with the positive and open treatment that they had received.

### **VI.iv.i.i Biomarker feedback in interventions**

Regarding the utility of fear appeals, such as the use of feedback of smoking-related exposure, risk or harm, there was a large overlap between the opinions of current and ex-smokers in this study and participants in previous qualitative studies, who had positively appraised this approach irrespective of ethnicity, age or geographic location of the sample (e.g. Kulwicki & Rice, 2003; McKie, Laurier *et al.*, 2003; Lai & Lau, 2005). Participants in the current study felt that interventions should be individualised - something which biomarker feedback can accomplish - and this sentiment was also expressed by participants in other studies (e.g. Butler, Pill *et al.*, 1998; Foraker, Patten

*et al.*, 2005). However, in contrast to earlier work, this study also showed that service users felt that carbon-monoxide increased their motivation to stop smoking. While it had been previously suggested to enhance individualised interventions by adding behavioural experiments (Kishchuk, Tremblay *et al.*, 2004), earlier studies have not been able to elucidate smokers' and ex-smokers' views on fear appeals in more detail.

It was obvious from the current study that participants felt a fine balance needed to be struck when administering fear appeals, especially those involving biomarker feedback. Participants reasoned while there will be those smokers who may not respond to this type of intervention at all (usually older smokers, who would have already sufficient evidence of the detrimental health effects of smoking but continued to smoke anyway), others may be terrified by the results of biomarker feedback. This may present a problem, especially when no adequate support is provided to either reassure smokers about the results or to equip them with the necessary prerequisites to stop smoking successfully. In contrast, some smokers, however, may believe that they are immune to the health effects of smoking if no sign of damage can be found. Thus such interventions may paradoxically reinforce smoking. These worries anticipate predictions from existing models of fear appeals, which will be discussed in the next chapter. Before considering the implications of participants' views for existing and future smoking cessation interventions, limitations of the current study need to be acknowledged.

### **VI.iv.ii Limitations**

This study was purposefully designed with a clear research agenda and analysis plan and took ample precautions to ensure both the reliability and validity of results (see VI.ii). However, the very nature of qualitative research, its context-dependency and focus on the idiographic level, necessarily limits the generalisability of findings and

thus ultimately their utility. The main methodological limitation of the current study, one that is a necessary consequence of qualitative research, relates to the sample. Participants were recruited from only two Stop Smoking Services, which were geo-and demographically very similar, thus reducing the extent to which findings can be extrapolated from this study to the broader context. However, the synthesis of qualitative studies has been suggested as one possible approach to overcome the limited generalisability of qualitative work (Noblit & Hare, 1988). For this reason, concurrent validity was sought by amalgamating findings with the existing literature, by placing accounts in their theoretical context and by evaluating both similarities and differences between earlier work and the current study so as to address this limitation.

### **VI.iv.iii Implications and conclusions**

There are a number of implications that can be gleaned from the results of this study. The arising typology and associated model describing the progression of participants towards cessation suggests that at the fundamental level smokers need to be made more self-aware so that they acknowledge, if not accept, the negative consequences of smoking - a finding, which contradicts the assumption that by now all smokers should be fully aware of the impact that smoking has on them and supports the continuing implementation of mass media campaigns to reach such 'hard-core' smokers or, in terms of the developed typology, 'committed smokers'.

An interesting upshot of this typology derives from the lack of awareness that was displayed by 'committed smokers' when it came to their own addiction to cigarettes. This would favour the use of behavioural experiments, such as asking smokers who have never attempted to quit to go without smoking for a day, so that these smokers can develop some awareness of both their addiction (as a first step towards considering



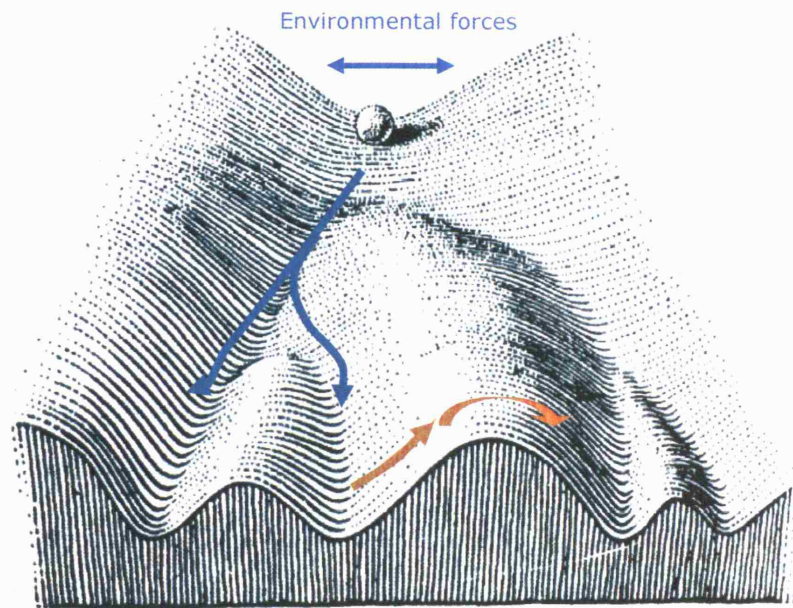
stopping) and realise the usefulness of smoking cessation medication for possible future quit attempts (which were generally negatively appraised by never quitters).

However, awareness alone is not sufficient to instigate cessation and some motivation is also required to drive and direct behaviour and thus lead to action. In agreement with theories of motivation, such as Prime Theory (West, 2006b), this motivation can be obtained from a variety of sources – both intrinsic and extrinsic. Thus, cessation can be construed as so called ‘evaluation-driven’ behaviour (relating to beliefs about what should be done) as is the case for ‘forced attempters’, or as ‘motive-driven’ behaviour (relating to anticipated positive feelings) as applies to ‘struggling attempters’. Either way, cessation interventions will need to increase the motivational forces that drive behaviour and the typology developed in this study would predict that some smokers may be more susceptible to extrinsically and some to intrinsically anchored approaches.

What will lead to long-term abstinence, however, is harder to deduce from the typology, and the model leaves open the possibility of people oscillating between being an unsuccessful and a successful quitter. One defining feature of smokers who eventually abstained for at least 6 months is best described as smokers experiencing a ‘Eureka’ effect, or, in Prime Theory terms, as reaching a ‘critical period’ in the epigenetic landscape that determines behaviour. Prime Theory posits that the development of a behaviour pattern is a dialectic process of dispositions interacting with events to change behaviour and further change dispositions. This process can be modelled by an epigenetic landscape, as seen in Figure VI.III, where a certain path or trajectory is followed until environmental forces push the path one way or the other at certain points (or forks) in ‘chreods’. Some chreods may be deep and the path followed will therefore be unaffected by small forces. However, positioning on the path may be such that travel

is 'on the cusp' (a critical period) of a chreod, when smaller forces may tip the path more easily one way or another. The 'classic' cross section of the chreod is curvilinear suggesting that a particular motivational force will have greater impact in individuals already close to the cusp leading to a sudden shift in disposition and thus behaviour.

**Figure VI.III Waddington's epigenetic landscape\***



\*Source: [www.primetheory.com](http://www.primetheory.com)

Thus one could speculate that in the current sample, this sudden shift towards cessation was associated with ex-smokers' description of accepting and taking responsibility for their own actions. Although such a process owing to its personal and highly subjective nature may not be easily instigated and integrated into an intervention, it would imply that approaches, which attempt to clarify and restructure cognitive patterns such as systemic or cognitive behaviour therapy, could prove fruitful for interventions if correctly tailored as, indeed, has been suggested elsewhere (Guichenez, Clauzel, Cungi, Guantin *et al.*, 2007).

However, while this progression towards accepting responsibility for one's own actions in general, and smoking in particular, may lead to an explicit shift in identity, this need not be the case. The model would predict that intrinsically driven rather than

extrinsically driven quit attempts would be more likely to result in such an identity shift.

With regard to smoking cessation interventions, it is suggested that no preference should be given towards emphasising external over internal reasons for quitting and vice versa. Thus in relation to the Stop Smoking Services some successful quitters will appreciate the competitive aspects of groups (extrinsic) and others will prefer to focus on themselves in small groups, or indeed individual therapy, to share their experiences (intrinsic).

In terms of increasing uptake of the Stop Smoking Services, there are two suggestions that arise from this study. First, there exists a need to overcome the negative stigma attached to the services. This may be achieved by changing the way that the services are advertised so that they appeal to a broader spectrum of potential users. For instance, smokers could be made aware that there is a choice between group and individual treatment and that counselling in the SSS differs from more traditional group counselling (e.g. for alcohol and drug dependence) as it focuses primarily on the behavioural element whereas other forms of counselling are much broader in approach by also including financial, psychosocial and legal issues.

Second, the SSS should be made more accessible by having rolling and ongoing groups, such that smokers are not bound by strict opening hours and can return when they feel the need to. In addition, increasing the number or locations of services by for instance introducing SSS in the workplace would make the services more opportunistic. While this will be costly, it may arguably be worth the additional expense to increase reach and recent guidance has endorsed this approach (NICE, 2007). With regards to the content and structure of the SSS approach, there were few consistent negative

comments and perhaps the most important one to consider is the reduction in group sizes to avoid unnecessary waiting times.

One particularly useful, effective aspect of the SSS, as perceived by service users, was carbon-monoxide feedback. Indeed, participants' positive appraisal of fear appeals in general, and biomarker feedback in particular, would seem to confirm the utility of this approach. Within the context of the extant typologies, personalising interventions should in theory help overcome the derogation of the smoking-health risk link by changing the awareness of smokers' own susceptibility to diseases, which were downplayed by never and unsuccessful quitters. In the light of participants' comments about the danger of scaring smokers without providing reassurance, the advantage of carbon-monoxide over other biomarkers, beside its low cost and easy implementation, is that it not only personalises risk and exposure information but also allows smokers who attempt to quit see an improvement in exposure levels following their behaviour change.

According to participants' responses, it would appear then that an intervention involving carbon-monoxide feedback may provide a useful addition to smoking cessation treatments outside the SSS, provided that this includes appropriate debriefing and provision of support (to ensure that smokers are not unduly scared) as well as a discussion of the future implications of results (to ensure that smokers will not feel invulnerable to the health risks). Chapter VII therefore reports on a trial of such an intervention, which was developed as an addendum to brief advice to test the efficacy of this approach.

## **Chapter VII**

### **Study 3: A randomised controlled trial of adding expired-air carbon monoxide level feedback to brief stop smoking advice – evaluation of cognitive and behavioural effects**

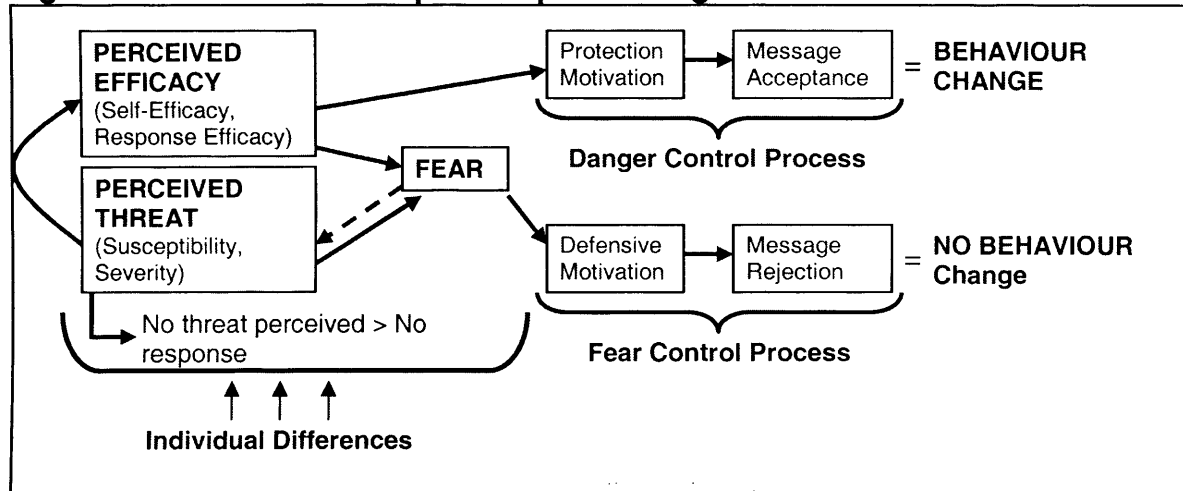
#### ***VII.i Introduction***

In Chapters II and III, the rationale for the use of exposure, risk and harm biomarkers in smoking cessation interventions was briefly discussed. As Chapter III indicates, results of studies assessing the utility of providing biomarker feedback to promote cessation have thus far been somewhat mixed. There is a theoretical rationale for including biomarker feedback in interventions. Health is often cited as one of the main reasons for smoking cessation (McCaul, Hockemeyer, Johnson, Zetocha *et al.*, 2006). For instance, it has been shown that worry and fear about health motivates behaviour change to reduce this threat (Cameron, 2003). It is clear that simply telling people they are at risk of developing a disease is rarely sufficient to change behaviour if they already know of the risk or if the risk refers to something happening in the future (Leventhal, Benyamini *et al.*, 1997). For this reason, making threatening information more salient, as is the case in fear appeals, has been proposed as a more effective approach (Witte & Allen, 2000). But what exactly comprises a fear appeal?

According to Rogers & Deckner (1975), a fear appeal is primarily characterised as a persuasive communication attempting to arouse fear, which in turn promotes precautionary motivation and self-protective action. The presence of threatening stimuli is meant to instil an unpleasant emotional state leading to increased motivation to alleviate this negative drive state, requiring appropriate responses at cognitive, affective

and behavioural levels. It is usually modifications at the behavioural level which are the target of fear appeals and according to McGuire's (1969) information-processing theory these are determined by the cumulative effect of communication on response variables, such as attention and comprehension: the higher the impact evoked, the greater the likelihood of behavioural changes.

**Figure VII.I: The extended parallel processing model**



Adapted from Witte (1998)

A number of models have been used to explain the likely mode of action in fear appeals; social cognition models have been particularly helpful, and indeed ubiquitously used, for elucidating how fear appeals can change health behaviours. More specifically, as elaborated in the Extended Parallel Process Model (EPPM, Witte, 1992), which is primarily based on - and unifies - the earlier Parallel Response Model (Leventhal, 1970) with Protection Motivation Theory (Rogers, 1975; 1983), fear appeals trigger coping responses, such as fear control and danger control. As shown in Figure VII.I people engage in protective behaviour and danger control only when they perceive themselves to be susceptible to severe threats (threat appraisal) and feel that they are able to perform a behaviour (i.e. display self-efficacy) that is effective (i.e. has response efficacy) in averting this risk (efficacy or coping appraisal). If no threat is perceived, there is no response to the fear appeal but when people perceive a threat and positively

appraise their efficacy to avert this threat, they are motivated to protect themselves and thus accept the fear appeal message.

However, threat in the absence of a sufficient level of self-efficacy is unlikely to increase motivation to stop smoking (Bishop, Marteau, Hall, Kitchener *et al.*, 2005). Indeed, it could result in the opposite effect because low efficacy appraisal leads to an increase in fear levels according to the EPPM. Consequently, a person will become defensive and be more concerned with managing their fear rather than the causes of their fear and therefore primarily concentrates on reducing this fear level by ignoring information and disengaging from the danger control process (see Figure VII.I). Thus fear arousal may have inhibiting as well as facilitating effects on the development of protection motivations (Ruiter, Abraham, & Kok, 2001); such fear control processes will usually result in threat message rejection, which means that no behaviour change ensues (Witte, 1992). It is therefore important to both increase people's perceptions of threat, thus raising worry levels, as well as to amplify efficacy in order to instigate behaviour change. As implied by the EPPM, all of these processes are of course also dependent on and affected by individual differences.

Social cognition models have been comprehensively studied and tested (Armitage & Conner, 2000); on the whole the utility of their constructs is corroborated by the evidence (Ruiter, Abraham *et al.*, 2001) with efficacy components emerging as the strongest determinants of protective action (Milne, Sheeran, & Orbell, 2000). When applying population level models to individual behaviour it is important, however, to be aware of the potential incongruence between what can be observed correlationally in epidemiological time-trend analysis and what determines a single person's behaviour (Piantadosi, Byar, & Green, 1988). This so-called 'ecological fallacy' can undermine

the validity of social cognition models, which may in part be informed by population-based studies and therefore individual-level studies are required to verify these findings and inform theory further. For instance, a recent study found that outpatients at a CVD clinic who were smokers and received biomarker feedback were more likely to have an increased intention to stop smoking after the intervention but only if their self-efficacy levels were high (Shahab, Hall, & Marteau, 2007). As fear appeals in part depend on these extrinsic, mostly intransigent, factors, their effectiveness, especially in smoking cessation, is not unequivocally supported by the evidence (Krugman, Fox, & Fischer, 1999). However, the impact of fear appeals has been linked not only to efficacy measures but also to other factors; for instance, it has been found that the way information is presented and the modality in which this occurs affect outcome (Keller & Block, 1996). The clearer and less abstract the message, the more likely it is to be noticed and acted upon (Backer, Rogers, & Sopory, 1992). It is evident that multiple emotions (e.g. sadness, anger, disgust) are elicited from fear appeals, but fear appears the force driving the action (Witte, 1998). Evidence from a meta-analysis suggests that the stronger the fear reaction, the higher the likelihood of a desired effect (Witte & Allen, 2000).

Yet, there is some controversy regarding the exact role of fear in fear appeals (Ruiter, Abraham *et al.*, 2001). It is widely accepted that emotions influence cognitions, in particular attention, memory and reasoning (Dolan, 2002). The literature suggests that emotion primarily involves the limbic system (LeDoux, 1996); more specifically, fear induction has a strong association with the amygdala (Phan, Wager, Taylor, & Liberzon, 2002). As exposure to fear-eliciting stimuli leads to increases in cortisol releasing hormone and norepinephrine in parts of the brain that play a role in information retention, namely the amygdala and hippocampal areas (Cook, 2002), it has been



postulated that the arousal produced by these effects may enhance memory for anxiety-inducing events (Erickson, Drevets, & Schulkin, 2003). On the basis of these well-corroborated findings, Keightley and colleagues (Keightley, Winocur, Graham, Mayberg *et al.*, 2003) have proposed that the amygdala and related regions found to be modulated by cognitive and emotional processing like the medial prefrontal cortex (Drevets & Raichle, 1998) and the anterior cingulate cortex (Esslen, Pascual-Marqui, Hell, Kochi *et al.*, 2004), form a primitive neural system for processing emotional stimuli.

While neurophysiological evidence provides good support for the existence of an emotion or fear network in human neural substrate, how do these findings translate from a computational to a more cognitive-functional level of analysis, i.e. the level of psychological theory? A promising approach originally derives from work on phobias in abnormal psychology. The emotional processing model (Foa & Kozak, 1986) proposes that emotions are represented by information structures in memory, an emotion network. Emotional processing (hereafter EP) itself is defined as a process whereby this network is activated and emotional disturbances are absorbed, thereby declining to the extent that behaviour can proceed without disruption (Rachman, 1980). Fear structures are thought to be propositional in nature (Lang, 1979) carrying interpretative information about the feared stimulus situation and about verbal, physiological and overt behavioural responses to it. This fear memory structure is not entirely accessible to consciousness; however, in line with connectionist principles, it can be activated through the presentation of fear-inducing material, which provides the necessary arousal. Only when the fear structure is activated, can it be modified and EP may occur. During activation, the provision of fear congruent or incongruent material is then thought to either strengthen or weaken the respective fear structure (Foa & Kozak,

1986). The general outline of this theory is supported by the success of exposure therapy in treating various phobias (Barlow, 1988) and by the salubrious effects of EP that occur in the emotional writing paradigm<sup>38</sup> (Pennebaker, 1997).

Against this background, stimuli that lead to greater arousal are postulated to be particularly successful for instigating emotional processing and thus behaviour change. However, as described above, in the context of smoking, self-efficacy has been argued to be instrumental to the way in which fear impacts on subsequent behaviour (Dijkstra & Brosschot, 2003). High self-efficacy may guide worriers<sup>39</sup> to a behavioural solution (cessation), thus underlining the constructive and adaptive nature of fear, whereas low self-efficacy and high disengagement beliefs (distortion or denial of the meaning of threatening information; Bandura, 1986) may lead smokers to the cognitive solution described by Borkovec (1998), i.e. avoidance. Thus the exact role of fear in motivating and initiating behaviour change has yet to be properly delineated though it seems that it is only avoidant, pathological worry or fear that proves maladaptive in the framework of fear appeals and EP theory.

### **VII.i.i Rationale**

Based on the reviewed fear appeal and emotional processing literature, it is suggested that fear appeals function by their ability to access neurologically based cognitive fear networks through increased physiological arousal and the provision of incongruent health-related information, thereby initiating EP as expressed by increased fear levels. Biomarkers, as one form of fear appeal, are thought to achieve this due to the nature of the stimulus provided; by personalising information, they counteract perceptions of

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<sup>38</sup> The emotional writing paradigm is the regular (usually written) recording of emotionally up-setting or involving events at the end of each day

<sup>39</sup> In the context of this chapter, health-related worry is considered interchangeable to health-related fear as both concepts are linked to specific outcomes (e.g. airways disease). This is in contrast to the concept of pathological worry (or 'rumination'), which is considered to be generic and not bound to a specific outcome (e.g. see Segerstrom, Tsao, Alden, & Craske, 2000)

invulnerability to the health consequences of tobacco-use, which are common among smokers (Strecher, Kreuter, & Kobrin, 1995), thus raising arousal levels and threat perceptions. Socio-cognitive models of persuasion like the elaboration likelihood model (Petty & Cacioppo, 1986) would predict that only messages that are considered relevant for oneself are thoroughly analysed and thus lead to stronger changes in attitudes, which would favour personalised feedback. Furthermore, while biomarkers may provide confirmation of exposure and thus possible harm caused by smoking, they are also helpful in evidencing positive changes in the body after smoking cessation, which would increase a smoker's perception of the response-efficacy of cessation. Lastly, biomarkers provide a clear and coherent message about the inherent harm associated with exposure to smoking, which should reduce the likelihood of the threat message being derogated.

A commonly used and easily accessible exposure biomarker is expired-air carbon-monoxide. In contrast to other biomarkers, determining carbon-monoxide levels is quick, relatively inexpensive and not invasive, making it an ideal addendum to existing interventions. As discussed in Chapter III, feedback of carbon-monoxide levels on its own has had only limited success in changing smokers' behaviour but tends to result in differences in smoking cessation rates when compared with a minimal control condition. Carbon-monoxide levels are routinely assessed in UK smoking cessation services (McNeill, Raw *et al.*, 2005), and as the qualitative analysis in Chapter VI shows, many smokers find this aspect of the services very helpful. However, what results mean in terms of risk for subsequent disease is currently not incorporated in treatment services and providing such tailored advice may offer an opportunity for further increasing motivation to stop smoking. Moreover, due to the simplicity of this intervention it may also be a useful addition to brief advice by physicians; considering

the large target population to which physicians have access, even small changes in treatment response could have a large impact at the national level (Raw, McNeill, & West, 1998). This randomised trial therefore aimed to assess the efficacy of adding tailored carbon-monoxide feedback to brief standard quit advice to test predictions of EP theory and its effectiveness both in the short- and long-term. In addition, this mixed (within and between factors) design study also explored possible causal pathways postulated by the extended parallel processing model (EPPM) and for this purpose a leaflet was developed to alter threat and efficacy perceptions over time with the aim of increasing motivation to stop smoking among all participants.

### **VII.i.ii Hypotheses**

Specifically, the following primary hypotheses were tested:

1.) Impact of leaflet - Providing the leaflet will

- a.) alter efficacy perceptions (increase perceived response and self-efficacy levels)
- b.) alter threat perceptions (increase perceived severity and susceptibility levels)
- c.) increase intention to stop smoking

2.) Impact of biomarker (CO) feedback (cognitive outcomes) - Providing additional personalised vs. generic quit advice will lead to greater increases in

- a.) perceived susceptibility to airway diseases
- b.) fear levels regarding airway diseases
- c.) intention to stop smoking

3.) Impact of biomarker (CO) feedback (behavioural outcomes) - Participants receiving CO feedback vs. no CO feedback will be more likely to have

- a.) engaged in smoking cessation behaviours
- b.) attempted to quit
- c.) stopped smoking completely at the 6-month follow-up

In line with predictions from the EPPM and EP, the following secondary hypotheses were also tested:

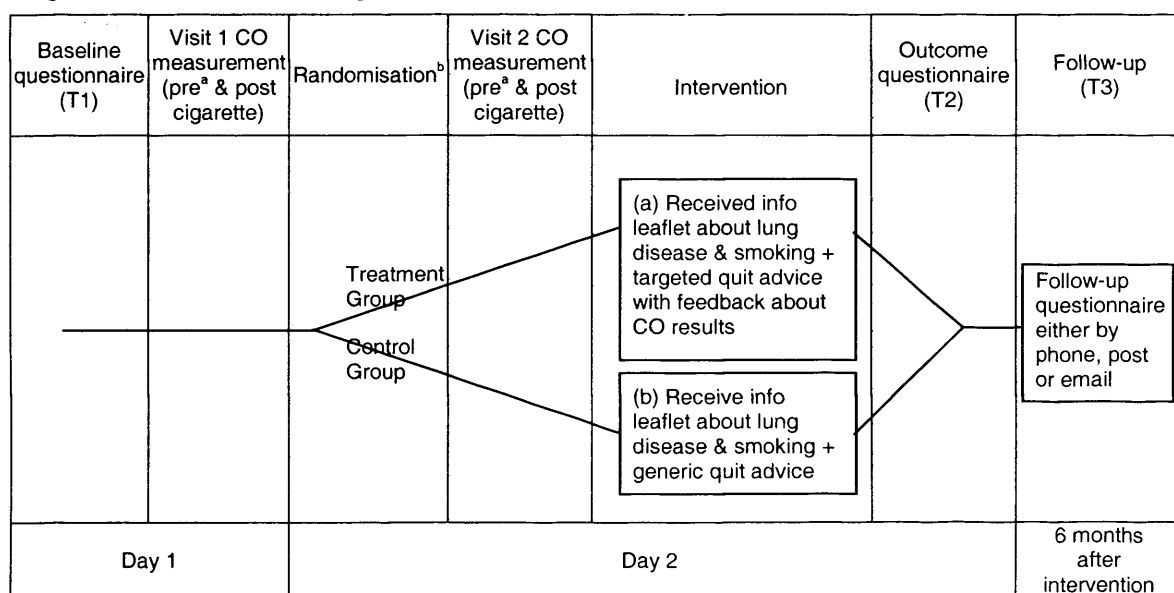
- 4.) Initial fear levels are higher among those who engage in smoking-related behaviour change at follow-up
- 5.) Perceived self-efficacy moderates the impact of the intervention on smoking-related behaviour change

## VII.ii Methodology

### VII.ii.i Procedure

This randomised controlled trial was carried out as part of study that assessed the differential exposure of smokers to carcinogens such as polycyclic aromatic hydrocarbons and tobacco-specific *N*-nitrosamines<sup>40</sup>.

**Figure VII.II: RCT design flow chart**



<sup>a</sup>Smoke-abstinence 30 min before <sup>b</sup>Randomisation is computerised (sealed envelope containing allocation to either control or treatment group)

Participants visited the laboratory on two occasions, 24 hours apart. At the first visit, the main purpose of the study, as pertaining to the measurement of exposure to carcinogens, was explained (see Appendix VII.I for the participant information sheet) and participants were asked to sign a consent form before urine and saliva samples were

<sup>40</sup> This study follows a similar design to the study reported in Chapter V

collected (see Figure VII.II for details of study design). At this stage participants also completed the baseline questionnaire (T1). Following the questionnaire, smokers were instructed to provide a breath sample by blowing into a breathalyzer that analyses carbon-monoxide content. Since alveolar carbon-monoxide levels change relatively rapidly with exposure to cigarette smoke, participants were asked to refrain from smoking half an hour before each laboratory sessions so as to obtain a standardised carbon-monoxide level at the pre-cigarette reading. After the first carbon-monoxide reading was taken, participants were asked to smoke a cigarette through a portable smoking topography device, the CReSSmicro<sup>®</sup> machine (Plowshare Technologies, Inc. Baltimore, Maryland; see Chapter V for details) in order to estimate puffing behaviour. Within 2 minutes of having smoked the cigarette, participants gave a second breath sample. At the end of the first session, participants were then provided with the portable smoking topography device and asked to continue smoking every cigarette through the machine until the following day, 24 hours later.

At the beginning of the second visit, participants were randomly allocated by means a random number generator to either the control or treatment condition before urine, saliva and breath samples were collected and participants were asked to smoke another cigarette through the CReSSmicro. In both the control and experimental group, participants were provided with a leaflet about lung disease and smoking. The control group received standardised, generic quit advice (“I would urge you to stop smoking; quitting is the single-most important thing you can do to feel better & improve your health”). By contrast, in the treatment group participants also received brief targeted feedback about their CO levels in relation to the development of cardiovascular and respiratory diseases (see Appendix VII.II for the intervention script).

At the end of the study, all participants completed the outcome questionnaire (T2); received a debriefing letter (in the treatment group with the personalised CO reading, see Appendix VII.III); were asked to consent to being contacted for a follow-up phone call and received £50 for their time. Six months after the second laboratory visit, participants were contacted by a researcher blinded to group allocation. If participants did not answer their phone on more than three occasions, they were contacted by email, and if this failed, by post. The follow-up questionnaire (T3) assessed a variety of measures including current smoking status, smoking cessation behaviours and intention to quit. The study received ethical approval from the UCL Ethics Committee (see Appendix VII.IV).

### **VII.ii.ii Power calculation**

Power calculation was performed using Gpower (Faul & Erdfelder, 1992). Based on a previous studies with similar measures and intervention design (Hall, Bishop, & Marteau, 2003; Hall, Weinman *et al.*, 2004; Shahab, Hall *et al.*, 2007), the effect size for cognitive (efficacy and threat perceptions) and behavioural (smoking cessation) group differences were estimated to be of a medium-to-large size<sup>41</sup> (Cohen's  $d \sim 0.5-0.7$ ). In order to detect such an effect in a two-tailed comparison of means or proportions with 80% power and a standard Type I error rate ( $\alpha=0.05$ ), a total sample of at least 128 participants would be required to detect differences at the lower end of the effect size range. As previous research in this area (Brown, Kahler, Niaura, Abrams *et al.*, 2001; Bovet, Perret, Cornuz, Quilindo *et al.*, 2002) estimated attrition to be low for 6-month follow-up (less than 10%), assuming a conservative attrition rate of 20%, would indicate a necessary total sample size of 160 participants for this study.

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<sup>41</sup> However, smaller effect sizes are still likely to be clinically significant

**VII.ii.iii Participants**

Participants were recruited through advertisements in local newspapers, flyers, emails, or posters on public bulletin boards at and around University College London. Smokers who responded to the advertisements were screened for eligibility through a telephone interview. Participants were included if they were between 18 and 60 years of age, smoked more than five cigarettes daily for the past year, and had been a regular smoker of one particular cigarette or hand-rolling brand for more than 3 months. Smokers were ineligible if they had a history of lung or heart disease or if they were pregnant.

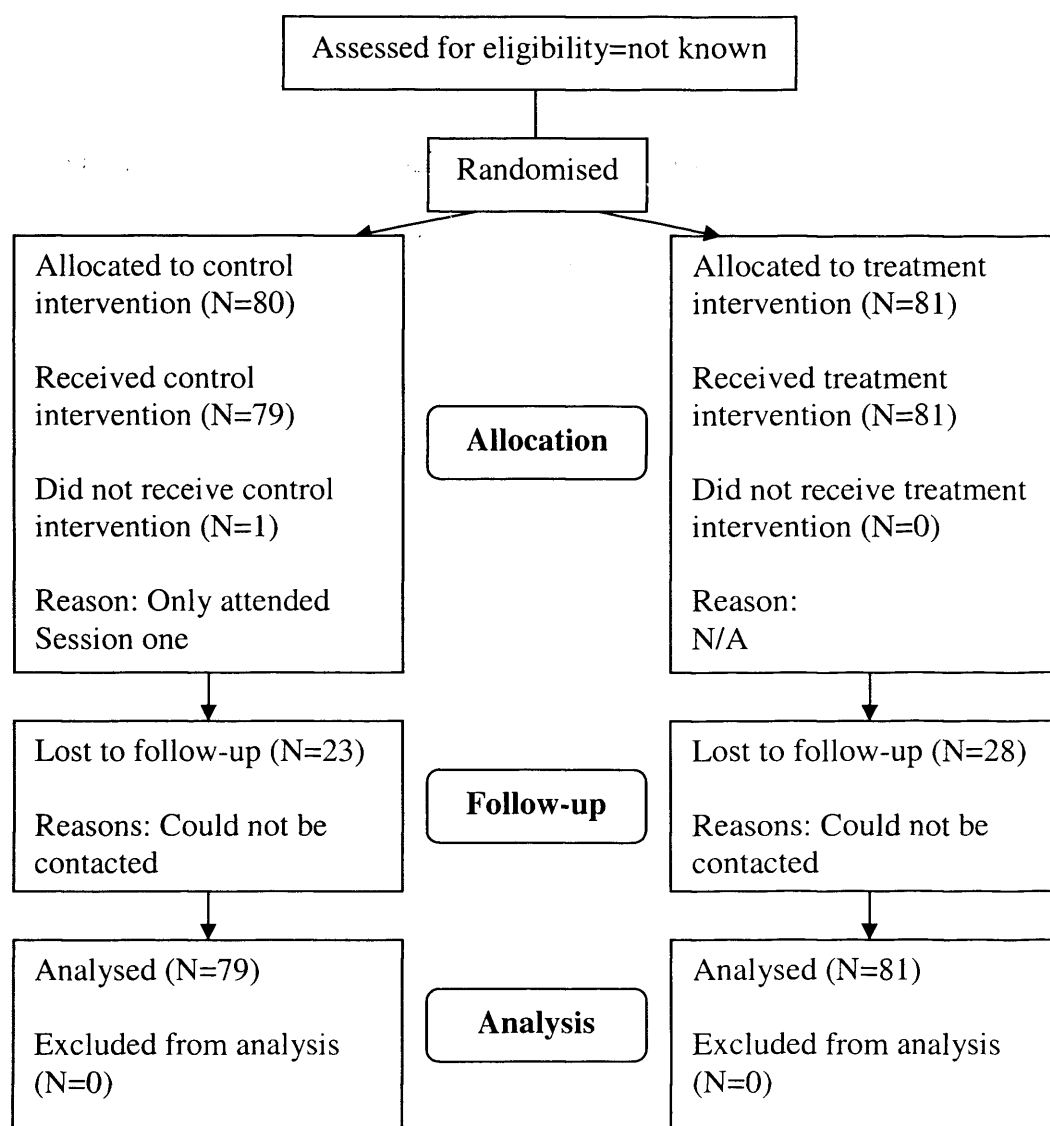
**Figure VII.III: Participant flow chart**



Figure VII.III provides an overview of participant retention across the study. Altogether, 32% of participants were lost to follow-up (somewhat more than anticipated<sup>42</sup>), and there were no significant differences between groups in terms of attrition. Participants lost to follow-up did not differ on any of the assessed demographic or cognitive variables other than age; those lost to follow-up were younger than those who remained in the study ( $t(119)=2.2, p=0.027$ ).

### **VII.ii.iv Leaflet**

A leaflet was developed (see Appendix VII.V) and piloted on smokers attending a smoking cessation clinic in North London between January and February 2006.<sup>43</sup> This leaflet contained information about the link between smoking and respiratory illnesses and was designed to increase smokers' awareness of both the seriousness of these diseases and their risk of developing diseases thus manipulating perceived severity and susceptibility. In addition, the leaflet also contained information about the effectiveness of smoking cessation for preventing smoking-related diseases (thus attempting to raise perceived response efficacy) as well as practical information about how to get support for quitting smoking (attempting to raise perceived self-efficacy).

### **VII.ii.v Intervention**

In addition to the leaflet, smokers in the experimental group also received brief targeted feedback that related their carbon-monoxide reading to cardiovascular, malignant and non-malignant lung diseases. The intervention schedule is provided in Appendix VII.II. A researcher described how carbon monoxide (CO) from smoking causes damage and how it relates to smoking intensity and thus disease risk. Participants in this group were also given a print-out that included their personal CO level in order to make the result

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<sup>42</sup> This reduces the power to detect medium-sized effects at the lower (Cohen's  $d \leq 0.45$ ) but not upper end (Cohen's  $d \geq 0.55$ ) to below the conventional level of 80%

<sup>43</sup> As piloting was anonymous and did not meet standard definitions of 'research', no ethical approval was required

more salient. The intervention was aimed to increase smokers' perception of their own susceptibility to smoking-related diseases and thus raise worry levels regarding smoking in order to increase quit intentions and motivate cessation.

### **VII.ii.vi Measures**

#### **VIII.ii.vi.i Cotinine**

Saliva samples were collected using a dental roll, which participants were asked to keep in the mouth until saturated. Samples were assayed for cotinine, a major metabolite of nicotine that provides a very sensitive and specific quantitative measurement of tobacco intake, using rapid gas-liquid chromatography (Feyerabend & Russell, 1990).

#### **VIII.ii.vi.ii Expired air carbon-monoxide**

A standard monitor (Smokerlyzer<sup>®</sup>, Bedfont Scientific Ltd, Kent, UK) was used to obtain breath carbon monoxide levels. A reading was taken on two different machines after a half-hour interval of not smoking and again within two minutes of having smoked a cigarette. Pre-cigarette readings were subtracted from the post-cigarette reading to determine CO boost. CO boost has been found to correlate with nicotine intake and intensity of smoking (Wood, Wewers *et al.*, 2004). In addition, both CO boost and the magnitude of carbon monoxide levels has been related to a number of lung diseases including COPD, cystic fibrosis and asthma (Kharitonov & Barnes, 2002) as well as lung cancer (Law, Morris *et al.*, 1997) and carbon-monoxide is one of the main cigarette constituents involved in cardiovascular disease (Ludvig, Miner, & Eisenberg, 2005).

#### **VIII.ii.vi.iii Questionnaire items**

This study used three questionnaires (T1, T2, & T3, see Figure VII.II and Appendix VII.VI). The baseline questionnaire T1 asked for information on participants' smoking history, quit attempts, future quit plans, as well as general demographic information. Deprivation level was determined using the Index of Multiple Deprivation (IMD), a

reliable measure of relative poverty based on post codes (Jordan, Roderick, & Martin, 2004). Body mass index (BMI) was calculated from participants' self-reported height and weight ( $\text{kg/m}^2$ ). In addition, the following constructs were assessed:

### *Nicotine Dependence (T1)*

The Heaviness of Smoking Index, (HSI, Heatherton, Kozlowski *et al.*, 1989) is a short version of the Fagerström test for nicotine dependence. The HSI is derived from the time to the first cigarette ( $\leq 5$  min=3 points; 6-30 min=2 points; 31-60 min=1 point;  $>60$ =0 points) and cigarettes per day (1-10=0 points; 11-20=1 point; 21-30=2 points;  $>30$ = 3 points) producing a scale from 0 to 6 with higher scores indicating greater dependence on nicotine.

### *Intention to stop smoking (T1, T2, T3)*

This measure assesses the intention of participants to stop smoking next month on two 7-point Likert response scales ranging from 'very unlikely' to 'very likely', and 'definitely will' to 'definitely will not'. This produces a mean score of intention, which has been shown to provide good reliability (Hall, Bishop *et al.*, 2003).

### *Fear (T1, T2)*

Fear (or worry) about smoking was assessed using two questions on 7-point scales with content-specific anchors regarding airway disease ('not at all afraid' and 'very afraid'; 'not at all worried' and 'extremely worried'). As previously shown (e.g. see Dijkstra & Broesschot, 2003), this item score possesses high reliability.

### *Perceived Severity and Perceived Susceptibility (T1, T2)*

Both constructs were derived from protection motivation theory (Rogers, 1975) and assessed by two single 7-point response scales, each with content-specific anchors regarding airway disease that have been successfully used in similar form before (Hall, Weinman *et al.*, 2004). For perceived susceptibility, participants were asked to rate their likelihood as well as risk (in comparison with non-smokers) of developing airway

disease (from 'very unlikely' to 'very likely' and 'much higher' to 'much lower', respectively). For perceived severity, participants were asked whether they believed that airway disease was either a serious or severe illness (from 'strongly agree' to 'strongly disagree').

### *Perceived Response Efficacy and Self-Efficacy (T1, T2)*

In the current study, both items were assessed by two 7-point rating scales, and the respective mean item score was used. Both measures have been shown to display good reliability (Hall, Bishop *et al.*, 2003). Response efficacy (the belief that something, e.g. a change in behaviour, can actually change a given outcome) was determined by asking smokers whether they believed that stopping smoking can reduce their risk or likelihood of getting airway diseases (from 'strongly agree' to 'strongly disagree'). Self-efficacy (the belief that oneself can change something, e.g. a given behaviour) was assessed by asking participants how confident they are to be able to stop smoking (from 'very confident' to 'not at all confident'), and how easy it would be for them to stop smoking (from 'very easy' to 'not at all easy').

### *Smoking cessation behaviours (T3)*

This measure samples a range of possible smoking cessation behaviours (see questionnaire T3 in Appendix VII.VI for a list) that have been implied in people's transition from smoking to non-smoking in hospital-based interventions (Glasgow, Stevens, Vogt, Mullooly *et al.*, 1991). At follow-up, participants were also asked to indicate their current smoking status.

### **VII.ii.vii Contributors**

This intervention was designed by myself and part of a larger study conceived by Ann McNeill and myself. I analysed the data and wrote-up the study results. The intervention was carried out by Ann McNeill, Erdem Pulcu and myself.

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### **VII.ii.viii Analysis**

To inform subsequent analysis, parametric assumptions for continuous variables were tested looking at histograms as well as skewness and kurtosis of data<sup>44</sup> to assess normality of distribution and Levene's test to assess homogeneity of variance. For those variables that failed assumptions, results from parametric tests were confirmed with non-parametric tests and, in case of discrepancies, non-parametric results are reported. Group differences were tested with t-tests or, when controlling for confounders, ANCOVA, changes over time with paired t-tests and associations with Pearson correlation coefficient; where appropriate Mann-Whitney U, Wilcoxon tests or Spearman's rho were used to validate results. Logistic and linear regressions were used to predict behavioural outcomes using group, demographic and smoking variables as predictors. Where it was impossible to use regressions owing to non-normality, log-linear models were fitted to data in order to be able to estimate moderation effects. All analysis used an intention-to-treat approach (assuming no changes in drop-outs from last point of contact) unless otherwise stated. As this study was somewhat underpowered owing to attrition, results were considered significant at the unadjusted 5% level to reduce the possibility of a Type II error.

### **VII.iii *Results***

#### **VII.iii.i Description of sample**

The study sample was relatively young with a mean age of 31 and slightly more men than women (Table VII.I). Participants had been smoking for an average of 14 years, smoked nearly 14 cigarettes per day and over a third had at some point used marijuana. The majority had attempted to quit in the last five years but only a tenth agreed or very strongly agreed with the statement that they were intending to stop smoking in the next month. There were no significant differences on baseline demographic or smoking

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<sup>44</sup> Values between -1 and 1 were considered normal

characteristics between those participants randomised to the intervention and those randomised to the control group on any of the assessed variables (all  $p>0.10$ ). Likewise, there were no significant group differences in terms of baseline cognitive variables (all  $p>0.10$ ; see Table VII.II). In general, the sample had reasonably low perceived self-efficacy of their ability to stop smoking but high perceived response efficacy of the utility of stopping smoking for preventing airway diseases as well as high perceived severity and susceptibility of airway disease. In addition, participants in both groups reported being worried about smoking but had low intention to quit in the next month.

**Table VII.I: Baseline demographic and smoking characteristics by group**

	All smokers (N=160)	Intervention (N=81)	Control (N=79)
<i>Demographic data</i>			
Mean (SD) age	31.7 (10.7)	30.9 (10.7)	32.6 (10.8)
Percent (N) male	56.3 (90)	55.6 (45)	57.0 (45)
Mean (SD) IMD <sup>†‡</sup>	32.0 (13.1)	32.2 (13.3) <sup>~</sup>	31.7 (12.9) <sup>^</sup>
Mean (SD) BMI <sup>†</sup>	23.9 (4.0)	23.6 (4.1)	24.1 (3.8)
<i>Smoking data</i>			
Mean (SD) cigarettes per day	13.8 (5.9)	13.4 (5.8)	14.3 (6.0)
Mean (SD) length of time of smoking in years	14.3 (11.1)	13.7 (11.0)	15.0 (11.3)
Mean (SD) HSI <sup>†</sup>	2.4 (1.5)	2.3 (1.6) <sup>‡</sup>	2.5 (1.5) <sup>‡</sup>
Percent (N) smoking marijuana	36.9 (59)	42.0 (34)	31.6 (25)
Percent (N) quit attempt in last 5 year	56.3 (90)	54.3 (44)	58.2 (46)
Percent (N) Want to quit next month	11.3 (18)	11.1 (9)	11.4 (9)
Mean (SD) CO Boost (ppm)	4.7 (4.3)	4.4 (1.9) <sup>\$</sup>	5.0 (5.8)
Mean (SD) Salivary Cotinine (ng/ml)	286 (158)	273 (145) <sup>‡</sup>	298 (171) <sup>‡</sup>

<sup>†</sup>IMD: Index of multiple deprivation, BMI: Body mass index, HSI: Heaviness of smoking index; <sup>‡</sup>Missing cases are due to term-address postcodes provided by participating students (considered an unreliable marker of SES) <sup>~</sup>18 cases missing, <sup>^</sup>7 cases missing, <sup>\$</sup>2 cases missing, <sup>‡</sup>1 case missing

In order to evaluate the reliability of the scales used to assess these constructs, Cronbach's  $\alpha$  were calculated (see Table VII.II). With the exception of perceived susceptibility, all scales had good reliability ( $\alpha \geq 0.7$ ) and for this reason, results were

analysed for the individual subscales of perceived susceptibility, which either assessed susceptibility to airway diseases compared with a non-smoker (comparative susceptibility) or directly asked smokers whether they felt at risk of developing airways disease (direct susceptibility, see Appendix VII.VI for exact measures).

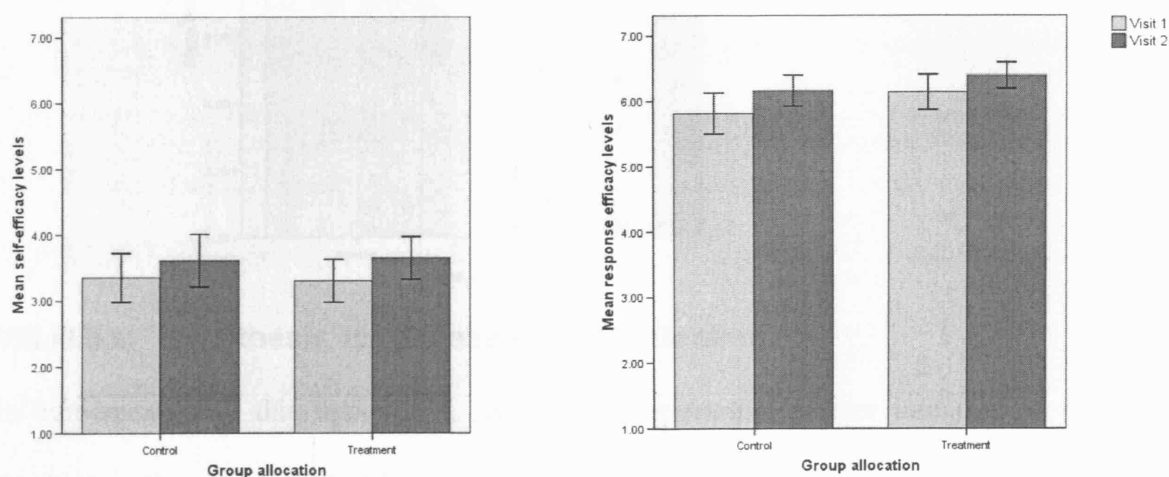
**Table VII.II: Baseline cognitive variables (on scale 1-7)**

	All smokers (N=160)	Intervention (N=81)	Control (N=79)
	Mean (SD)		
Perceived self-efficacy ( $\alpha=0.70-0.78$ )	3.3 (1.6)	3.3 (1.5)	3.4 (1.6)
Perceived response efficacy ( $\alpha=0.66-0.70$ )	6.0 (1.3)	6.1 (1.2)	5.8 (1.4)
Perceived susceptibility ( $\alpha=0.50-0.55$ )	5.2 (1.2)	5.2 (1.1)	5.3 (1.2)
Perceived severity ( $\alpha=0.82-0.84$ )	5.5 (1.9)	5.3 (2.0)	5.7 (1.9)
Fear/worry about smoking ( $\alpha=0.79-0.84$ )	5.1 (1.6)	5.0 (1.6)	5.1 (1.6)
Intention to quit in next month ( $\alpha=0.73-0.86$ )	2.8 (1.6)	2.8 (1.6)	2.9 (1.6)

### VII.iii.ii Impact of leaflet

#### VIII.iii.ii.i Hypothesis 1a: Increase in efficacy perceptions

**Figure VII.IV: Mean efficacy perceptions by group and visit**



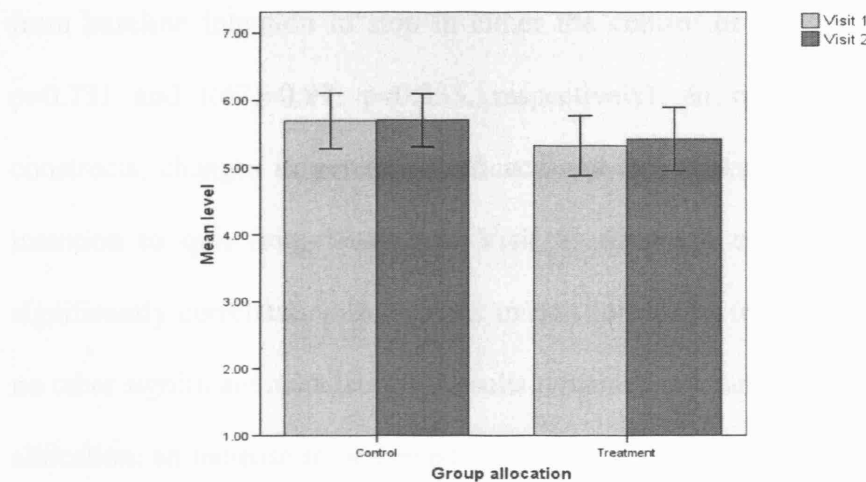
In line with predictions, there was a significant increase in perceived self-efficacy from visit 1 to visit 2 in the treatment group ( $t(80)=2.8$ ,  $p=0.006$ ) and in the control group ( $Z=-2.5$ ,  $p=0.012$ ). Response efficacy levels also significantly increased across visits in both

the control ( $t(78)=2.3$ ,  $p=0.023$ ) and treatment group ( $t(80)=2.1$ ,  $p=0.037$ , see Figure VII.IV).

#### VIII.iii.ii.ii Hypothesis 1b: Increase in threat perceptions

As predicted, there was a rise in susceptibility perceptions across visits in the control ( $t(78)=2.6$ ,  $p=0.01$ ) and treatment group ( $t(80)=5.0$ ,  $p<0.001$ ). This finding was confirmed when repeating the analysis for the subscales of comparative susceptibility ( $t(78)=2.1$ ,  $p=0.038$  and  $t(80)=3.0$ ,  $p=0.004$  for control and treatment group, respectively), while in the case of direct susceptibility there was a significant increase only in the treatment ( $t(80)=4.8$ ,  $p<0.001$ ) but not control group ( $Z=-1.8$ ,  $p=0.069$ ). However, contrary to expectation, severity perceptions remained similar across visits at a uniformly high level in both groups without a further increase after provision of the leaflet (see Figure VII.V).

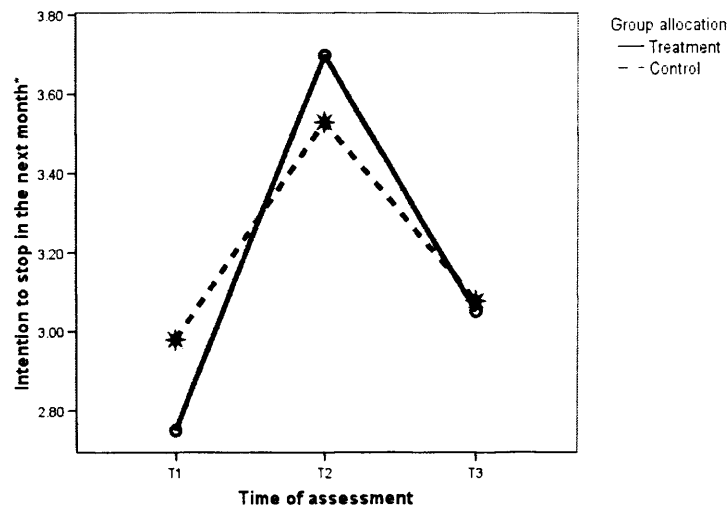
**Figure VII.V: Mean severity perceptions by group and visit**



#### VIII.iii.ii.iii Hypothesis 1c: Increase in quit intention

In agreement with this hypothesis, participants reported a greater intention to stop smoking in the next month at Visit 2 than at Visit 1, which applied to both participants in the control ( $t(78)=4.1$ ,  $p<0.001$ ) and treatment group ( $t(80)=7.0$ ,  $p<0.001$ ).



**Figure VII.VI: Changes in intention to stop smoking across time by group**

\*On scale from 1-7

However, looking only at participants with complete data and excluding quitters, at the time of the follow-up call, intention to stop smoking had dropped back to more or less previous levels for both groups (see Figure VII.VI) and was not significantly different from baseline intention to stop in either the control or treatment group ( $t(50)=0.34$ ,  $p=0.731$  and  $t(47)=0.97$ ,  $p=0.335$ , respectively). In order to evaluate the EPPM constructs, changes in perceived efficacy and threat were correlated with changes in intention to quit from Visit 1 to Visit 2. Although changes in self-efficacy were significantly correlated with changes in quit intentions ( $r=0.289$ ,  $p<0.001$ ), there were no other significant associations. Results remained the same when controlling for group allocation; an increase in perceived self-efficacy was associated with an increase in quit intentions across visits ( $r=0.288$ ,  $p<0.001$ ) but no other EPPM variable was associated with quit intentions.

### **VII.iii.iii Impact of biomarker feedback (cognitive outcomes)**

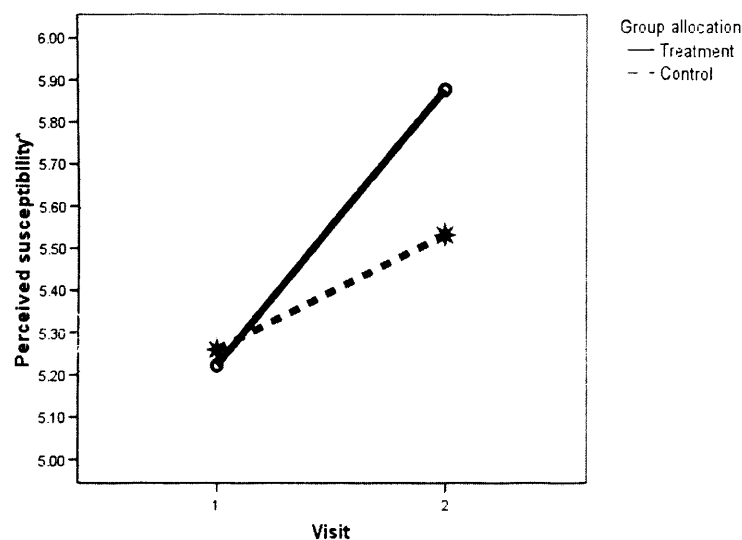
For this analysis, change scores were computed to assess interactions. Although an interaction could also be assessed with a repeated measures ANOVA, change scores

will yield equivalent results but have the advantage that they can also be used in non-parametric tests to determined interactions.

### VIII.iii.iii.i Hypothesis 2a: Increase in perceived susceptibility

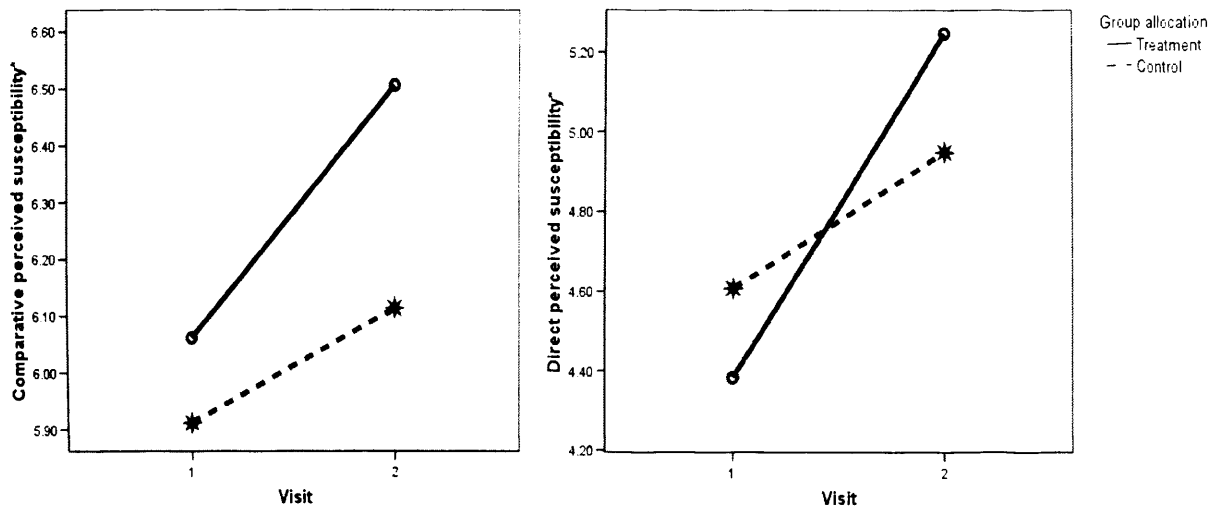
As predicted , perceived susceptibility to airway diseases increased more strongly in the treatment than in the control group across visits ( $t(151)=2.3$ ,  $p=0.023$ ; see Figure VII.VII).

**Figure VII.VII: Group by time interaction in perceived susceptibility**



\*On scale from 1-7

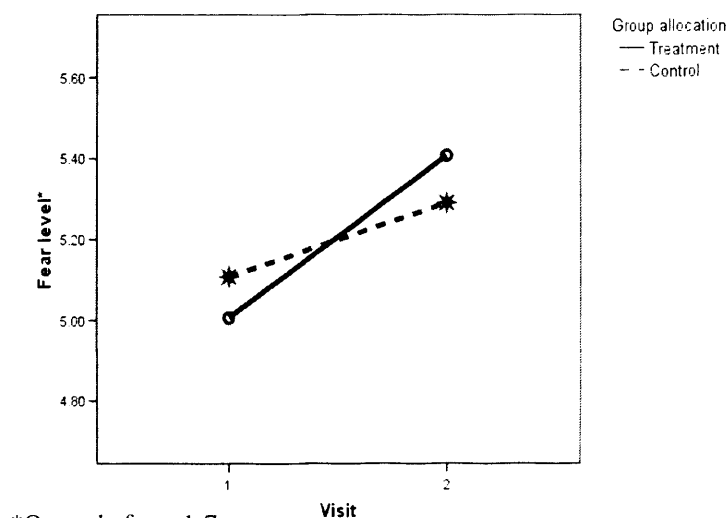
Since reliability of the susceptibility measure was low, the analysis was also repeated with the individual scales. Figure VII.VIII shows that the interaction effect disappeared when looking at the comparative measure of perceived susceptibility ( $t(136)=1.36$ ,  $p=0.175$ ) but remained present when susceptibility was assessed by asking smokers directly whether they agreed that they were at increased risk from diseases ( $t(158)=2.3$ ,  $p=0.026$ ).

**Figure VII.VIII: Comparative and direct perceived susceptibility by group and time**

\*On scale from 1-7

### VII.iii.iii.ii Hypothesis 2b: Increase in fear levels

Although paired t-test showed an increase in fear levels only in the treatment ( $t(80)=3.2$ ,  $p=0.002$ ) and not in the control group ( $t(78)=1.8$ ,  $p=0.076$ ) across visits (Figure VII.IX). ... contrary to expectations, the change in fear levels (as indicated by change scores) was not significantly different between groups ( $t(158)=1.4$ ,  $p=0.180$ ). In addition, changes in susceptibility were not associated with changes in fear levels in either treatment ( $r=0.080$ ,  $p=0.476$ ) or control group ( $r=-0.011$ ,  $p=0.925$ ). However, when looking across groups at those with low and high self-efficacy separately, there was a significant positive association of direct susceptibility with fear levels among the former ( $r=0.231$ ,  $p=0.046$ ) but not the latter group ( $r=-0.082$ ,  $p=0.458$ ).

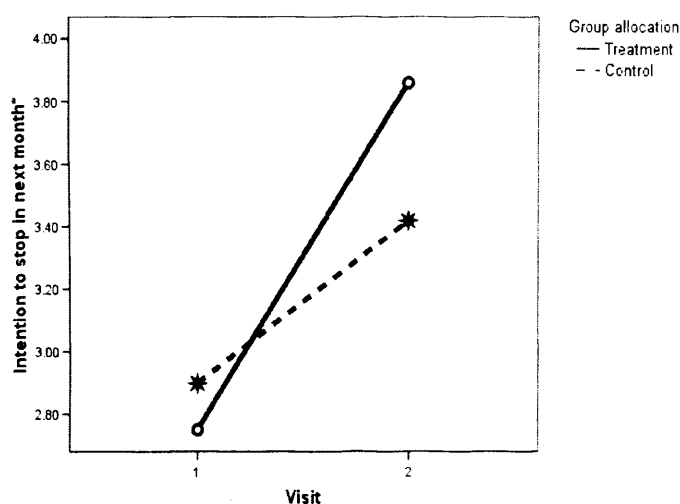
**Figure VII.IX: Fear levels by group and time**

\*On scale from 1-7

### VIII.iii.iii.iii Hypothesis 2c: Increase in quit intentions

As predicted, participants in the treatment group displayed a greater rise in their reported intention to stop smoking than those in the control group ( $t(151)= 2.9$ ,  $p=0.004$ ; see Figure VII.X).

**Figure VII.X: Group by time interaction in intention to stop smoking**



\*On scale from 1-7

### VII.iii.iv Impact of biomarker feedback (behavioural outcomes)

#### VIII.iii.iv.i Hypothesis 3a: Increase in smoking cessation behaviours

Half of participants at follow-up reported having engaging in at least one smoking cessation behaviour over the last six months, but contrary to expectations, there were no significant group differences in any individual smoking cessation behaviour (all  $p>0.10$ ). As can be seen in Table VII.III, every seventh smoker had either talked to their GP or another health professional (HP) about giving up smoking. One in fifteen smokers had made a phone call to a quit-line or had made an appointment and visited the smoking cessation services. A fifth of those followed up, who were current smokers, had set a date to stop, and one in eight had used medication to aid cessation. However, the most prevalent change in behaviour reported was the reduction in cigarette consumption<sup>45</sup>.

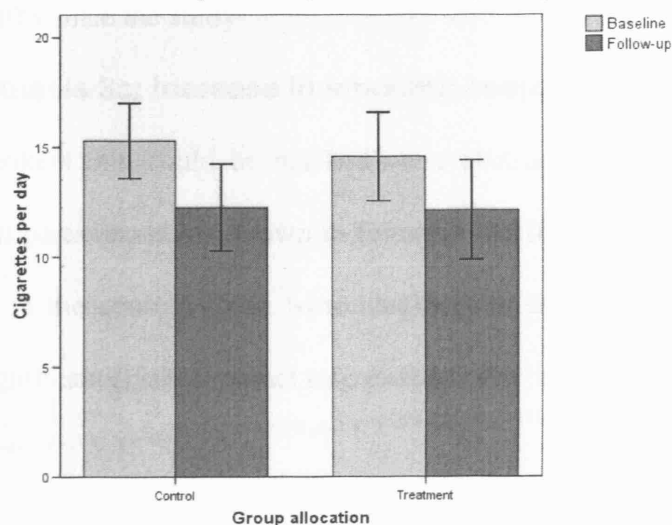
<sup>45</sup> Although cutting down is not a proper smoking cessation behaviour, it has been included in analysis as it can be considered as a step towards cessation indicative of a change in attitude (“cut-down then quit”)

**Table VII.III: Smoking cessation behaviours<sup>^</sup> by type and group<sup>#</sup>**

	All smokers (N=152)	Intervention (N=76)	Control (N=76)			
	Percent (N)					
Talked to GP about giving up smoking	14.5 (22)	14.5 (11)	14.5 (11)			
Talked to other HP about giving up smoking	13.8 (21)	10.5 (8)	17.1 (13)			
Telephoned smoking helpline	6.6 (10)	5.3 (4)	7.9 (6)			
Made appointment with/visited smoking cessation services	6.6 (10)	6.6 (5)	6.6 (5)			
Used smoking cessation medication (NRT/Zyban/Other)	12.5 (19)	9.2 (7)	15.8 (12)			
Set date to stop smoking	19.7 (30)	18.4 (14)	21.1 (16)			
Cut down cigarette consumption	35.5 (54)	32.9 (25)	38.2 (29)			
Any of the above cessation behaviours	46.7 (71)	46.1 (35)	50.0 (36)			

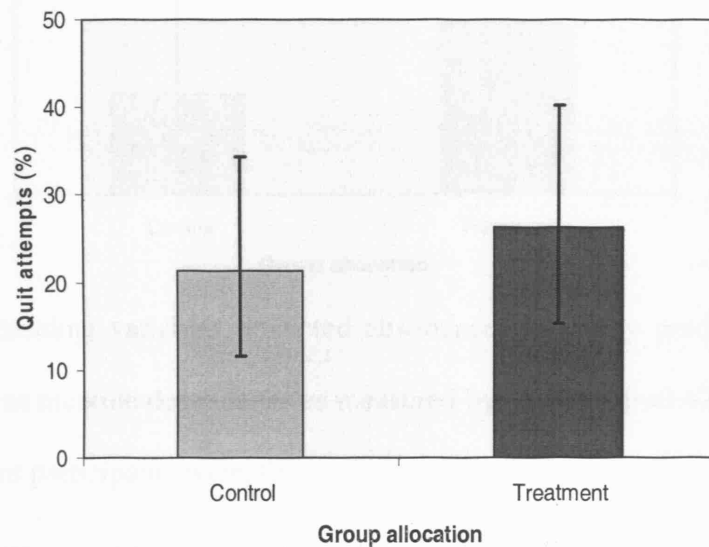
<sup>^</sup>Quit attempts are considered in the next section; <sup>#</sup>Excluding quitters (N=8)

Indeed, there was a significant decrease in cigarettes smoked per day from the start of the study to the follow-up (see Figure VII.XI) and this had occurred in both the treatment ( $t(46)=-3.0$ ,  $p=0.005$ ) as well as the control group ( $t(50)=-4.0$ ,  $p<0.001$ ). Overall, there were no significant differences in the mean number of smoking cessation behaviours reported between groups (0.97 (SD=1.4) and 1.27 (SD=1.9) for treatment and control group, respectively;  $t(150)=1.14$ ,  $p=0.257$ ).

**Figure VII.XI: Cigarette consumption by time and group**

**VIII.iii.iv.ii Hypothesis 3b: Increase in quit attempts**

As shown in Figure VII.XII, marginally more people in the treatment group (26.4%) attempted to quit than in the control group (21.4%) but this difference was not significant ( $\chi^2(1)=0.37$ ,  $p=0.542$ )<sup>46</sup>.

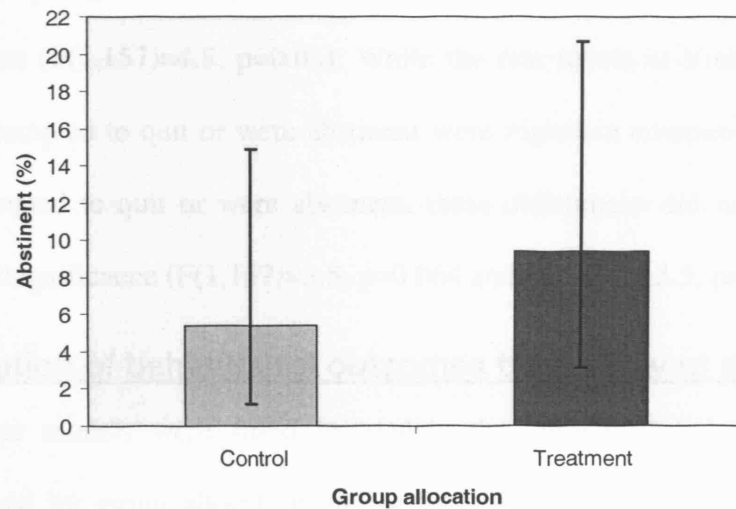
**Figure VII.XII: Quit attempts by group**

A forward conditional logistic regression was conducted to predict making a quit attempt and included group allocation as well as demographic and cognitive baseline variables. The only significant predictor of making a quit attempt at follow-up was past quit attempts ( $\beta=4.16$ ,  $p=0.036$ ).<sup>46</sup> Participants who said they had attempted to stop smoking in the last five years were also more likely to report having tried to stop smoking in the 6 months since the study.

**VIII.iii.iv.iii Hypothesis 3c: Increase in smoking cessation rate**

Overall, 7.3% of smokers that could be reached were abstinent at follow-up, which translates to 5% of all participants. As shown in Figure VII.XIII, although nearly twice as many smokers as in the control group were abstinent in the treatment group, this difference was not significant (Fisher's exact test,  $p=0.481$ )<sup>46</sup>.

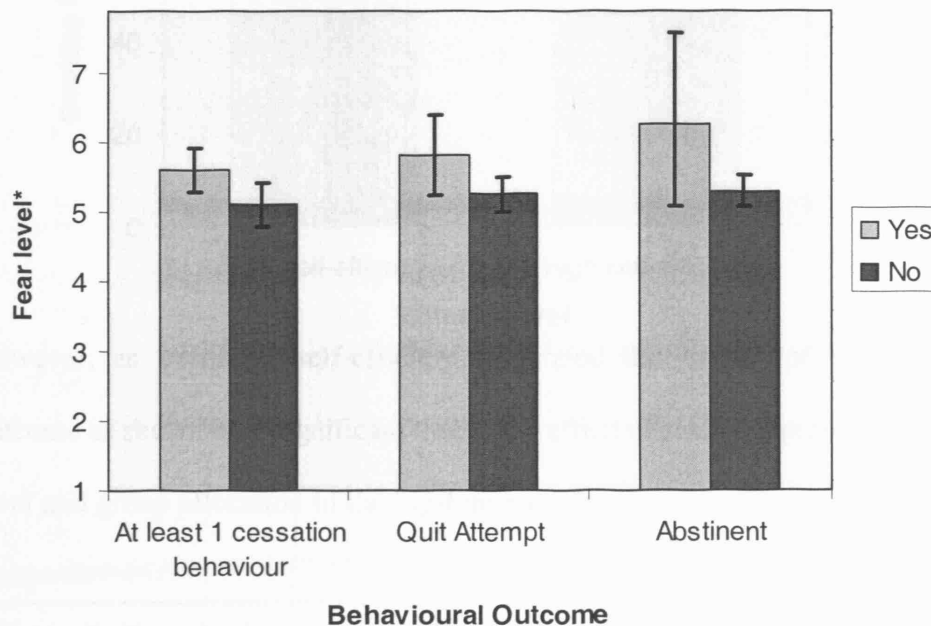
<sup>46</sup> The presented results here are not intention-to-treat, but intention-to-treat analyses were carried out to confirmed these results

**Figure VII.XIII: Smoking cessation by group among participants at follow-up**

None of the baseline variables predicted abstinence. The only predictor approaching significance was nicotine dependence as measured by the HSI ( $\beta=0.471$ ,  $p=0.074$ )<sup>46</sup>; the more dependent participants were, the less likely it was that they were abstinent.

#### **VII.iii.v Effect of fear levels on behavioural outcomes**

Since self-efficacy interacted with fear levels, it was entered as a covariate in an ANCOVA.

**Figure VII.XIV: Fear levels by behavioural outcomes**

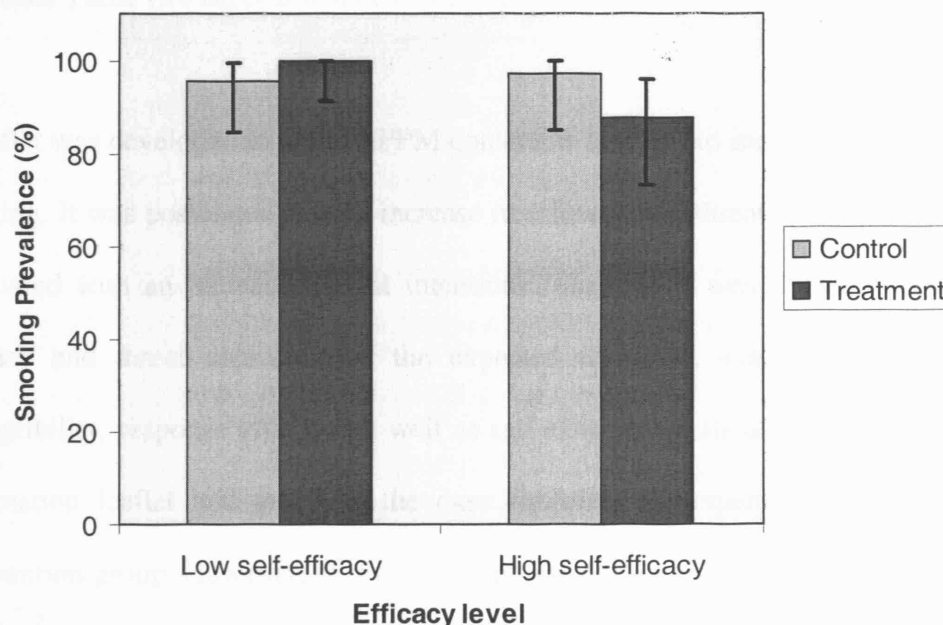
\*Estimated marginal means

As shown in Figure VII.XIV, in line with predictions, fear levels at Visit 2 were significantly higher among those, who subsequently engaged in smoking cessation behaviours ( $F(1,157)=4.8$ ,  $p=0.03$ ). While the fear levels at Visit 2 of those who had either attempted to quit or were abstinent were higher in comparison to those who had not attempted to quit or were abstinent, these differences did not reach conventional levels of significance ( $F(1,157)=3.5$ ,  $p=0.064$  and  $F(1,157)=3.5$ ,  $p=0.062$ , respectively).

### **Moderation of behavioural outcomes by perceived self-efficacy**

Log-linear models were fitted to explain the spread of behavioural outcomes as determined by group allocation and self-efficacy levels<sup>47</sup>. Results showed that self-efficacy did not moderate the impact of the intervention on either engagement in smoking cessation behaviours or making quit attempts.

**Figure VII.XV: Smoking prevalence by group and self-efficacy level**



However, as expected, self-efficacy moderated the impact of the intervention on outcome as shown by a significant three-way effect of smoking prevalence, self-efficacy level and group allocation in the log-linear model (Likelihood ratio  $\chi^2(1)=4.9$ ,  $p=0.027$ ,

<sup>47</sup> Since self-efficacy levels were not normally distributed and skewed towards the lower end of the scale, a median-split ( $<3.5$ ,  $\geq 3.5$ ) was carried out for the purposes of this analysis; in addition, since self-efficacy levels were manipulated, this analysis only considers self-efficacy at Visit 2 after the leaflet provision



see Figure VII.XV). Only in the intervention but not the control group were high self-efficacy levels associated with a greater quit rate (Fisher's exact test,  $p=0.026$ ). Indeed, in the intervention nobody with low-self-efficacy levels had quit. In addition, when only those with complete follow-up data and high self-efficacy levels were included in the analysis, there was a near significant effect of the intervention on smoking cessation when compared with the control group (Fisher's exact Test,  $p=0.078$ ).

### ***VII.iv Discussion***

The purpose of this pilot study was twofold. First, it aimed to delineate possible pathways to behaviour change as postulated in both the extended parallel processing model (EPPM) and the emotional processing model (EP). Second, it sought to evaluate the efficacy of providing personalised quit advice to smokers for motivating smoking cessation. These two aspects will be discussed in turn.

A leaflet was developed to target EPPM constructs in order to increase intention to stop smoking. It was postulated that an increase in efficacy and threat perceptions would be associated with an increase in quit intentions. The leaflet was effective in changing efficacy and threat appraisals in the expected direction; smokers reported higher susceptibility, response efficacy as well as self-efficacy levels after provision with the information leaflet and this was the case for both participants in the control and intervention group. However, severity perceptions did not change across visits in either group, which may have been due to a ceiling effect. Perceived severity of smoking-related diseases was already at a very high level at baseline, which will have rendered the detection of meaningful changes over time difficult. In addition, it is very likely that most smokers were already intimately aware of the severity of smoking-related diseases, either through personal experience from family and friends or through the media, and

especially so for airways disease as prominent as lung cancer, which this study focused on.

As expected, intention to stop smoking increased from Visit 1 to Visit 2 in both the treatment and control group. However, contrary to expectation, this change in quit intentions was only associated with perceived self-efficacy and not any of the other proposed cognitive precursors of behaviour change, i.e. perceived susceptibility, severity and response efficacy. This is in agreement with previous research, which has shown that self-efficacy is particularly instrumental for behaviour change (e.g. see Strecher, Devellis, Becker, & Rosenstock, 1986; Milne, Sheeran *et al.*, 2000). By contrast, the lack of an association of increased motivation to quit with other EPPM constructs would suggest that these may be more distal and thus of secondary importance for attitudinal and behaviour change. However, it should be noted that a possible ceiling effect<sup>48</sup> and low power to detect smaller effect sizes may have partly contributed to these results.

While the leaflet was successful in altering threat and efficacy perceptions as well as motivation to quit, these effects were short-lived. At the 6-month follow-up, intentions to stop smoking had returned to baseline levels. This implies that educational leaflets like the one used in this study may have some utility in raising awareness but that they are unlikely to lead to long-term attitudinal or behavioural changes; a finding, which has been observed in health behaviours other than smoking cessation (e.g. sun protection: Dey, Collins, Will, & Woodman, 1995; or medication adherence: Guilera, Fuentes, Grifols, Ferrer *et al.*, 2006).

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<sup>48</sup> As was shown in Table VII.II, all three constructs (perceived susceptibility, severity and response efficacy) had high baseline levels in contrast to self-efficacy

In line with predictions, personalised quit advice incorporating carbon-monoxide levels led to a more amplified change in perceived susceptibility in treatment group participants compared with the generic quit advice that was provided to control group participants, which corroborates suggestions that biomarker feedback reduces unrealistic optimism regarding the acquisition of smoking-related diseases (McClure, 2001). Moreover, as anticipated, showing smokers evidence of exposure to, and thus potential harm from, cigarette smoke increased their fear levels across visits but not significantly more than in the control group.

The concurrent increase in both fear and susceptibility levels in the intervention group relative to the control group is consistent with EP theory in that the presentation of CO levels (fear-inducing material) would have enabled access to the fear network (leading to increased fear levels), which could then, by presentation of incongruent material (the leaflet) be modulated to include new information resulting in changed threat perceptions (increased susceptibility). Although there was no association between rise in susceptibility perceptions and fear levels *per se*, self-efficacy levels affected this relationship – only among those with low self-efficacy levels was the increase in susceptibility levels associated with a corresponding increase in fear levels. In agreement with EPPM predictions, those smokers who perceived a greater threat (susceptibility) but felt they could do nothing to avoid the threat (displayed low perceived self-efficacy) became more worried as these threat perceptions fed back into the fear loop further increasing fear levels.

As postulated, providing personalised feedback increased participants' motivation to stop smoking in comparison with the control group. However, this change was not long-term and intention levels had fallen back to baseline values at the six months follow-up.

Indeed, at the six months follow-up there were no significant differences between the treatment and control group on any behavioural outcome variable. One striking finding was the unanimous reduction in cigarette consumption in both the treatment and control group from baseline levels, which may perhaps be related to increases in cigarette prices and the upcoming smoking ban in the UK at the time. Although more people in the treatment group attempted to stop smoking than in the control group, in contrast to previous studies using biomarker feedback (see Chapter III), this difference did not reach a significant level. However, consistent with earlier research (Sutton, 1994) past behaviour, i.e. attempting to quit in the last 5 years, was the strongest predictor of future behaviour, i.e. attempting to quit in the 6 months following the study.

In agreement with the EP model, when controlling for self-efficacy those people who had higher fear levels at the second visit were more likely to have taken some action and engaged in smoking cessation behaviours; there was also some indication that they were more likely to have attempted to quit smoking or to be abstinent at the follow-up.<sup>49</sup> This relationship between behaviour change and fear levels underlines not only the importance of the emotive and preconscious level over and above a purely semantic and intellectual understanding of the threat of smoking but also the motivating power of emotions for instigating behaviour change in order to alleviate the unpleasant state of fear (Easterling & Leventhal, 1989).

As hypothesised, a moderation effect of self-efficacy on the impact of the intervention was demonstrated; self-efficacy had a differential effect in terms of smoking cessation in the treatment and control group. Whereas in the treatment group there was a

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<sup>49</sup> In order to test this causal relationship, a mediation analysis would be required. However, since there were no significant group differences in terms of behavioural outcome, mediation could not be assessed.

significant difference in smoking rates between those with low and high self-efficacy, there were no such differences in the control group. Indeed, there was not one person with low self-efficacy to stop smoking in the treatment group. This finding would support the view outlined in the introduction that high self-efficacy may instigate behavioural (quit) and low self-efficacy cognitive (disengagement) solutions, therefore leading to improved outcome in only one of the sub-groups in the intervention. By contrast, in the control group, self-efficacy would not be expected to significantly moderate smoking cessation in the absence of sufficient threat appraisal (Witte, 1992); that is, since the intervention in the control condition was less intensive, perceived threat was only partly increased and therefore would be less likely to lead to further efficacy appraisal. In addition, there was a main effect of self-efficacy on motivation to stop smoking - those with high self-efficacy had stronger intentions to stop than those with low self-efficacy. This corroborates earlier studies demonstrating a similar effect and underlines the importance of self-efficacy for cognitive and thus behaviour change (e.g. Bishop, Marteau *et al.*, 2005; Shahab, Hall *et al.*, 2007)

Altogether, five percent of all participants were abstinent at the six months follow-up (or 7.3% of all those who were followed up), which is comparable to rates observed in some (Porter & McCullough, 1972; Page, Walters, Schlegel, & Best, 1986; Wilson, Wakefield, Steven, Rohrsheim *et al.*, 1990) but not most other studies that have looked at the effect of brief smoking cessation advice (Lancaster & Stead, 2004). In the treatment group, smoking cessation levels were somewhat higher than in the control group but still at relatively low levels of just above six percent (four percent in the control group) in the intention to treat analysis. There are a number of reasons for this. The sample was non-randomly recruited to participate in a laboratory study about smoking (not cessation) and were therefore unmotivated to quit; participants were also

comparatively young, both of which could have biased participants characteristics and may explain why cessation rates in the treatment and control groups were at the low end compared with similar interventions using biomarker feedback (see Bize, Burnand *et al.*, 2005).

The question remains, why did biomarker feedback only lead to short-term changes in cognitive antecedents of behaviour change but not to behaviour change itself? In part, the result may present an artefact of the study design; as discussed in the systematic review of this area in Chapter III, CO feedback has been shown to impact on smoking cessation when treatment and control conditions are not equally matched, that is when an intensive treatment is compared with a minimal control. However, in the current study both treatment and control conditions were maximally matched to clarify the effect of expired air carbon-monoxide. In addition, exposure biomarker feedback in the studies reviewed in Chapter III was generally provided to highly motivated populations. In contrast, smokers in the current study were not selected for their motivation to stop smoking. In fact, the opposite was the case; only regular current smokers were included with no emphasis being placed on motivation to stop smoking. Lastly, it could be speculated that alveolar CO levels may have failed to provide smokers with novel information (owing to growing awareness of the effects of smoking) and that the information may have been too abstract, remaining – as it did – at a purely numerical level, all of which may have reduced the potential impact of biomarker feedback.

Given these findings, biomarkers of actual harm incurred from smoking, as has been previously suggested (Hirschl, Francesconi, Chudik, Katzenschlager *et al.*, 2004), may perhaps offer a more promising approach to motivate smoking cessation; something, which could be evaluated in future research. As argued in Chapter II and III, imagery

has a more direct impact on cognitive and emotional processing than overt or covert language; it is to all intents and purposes more intrusive and therefore less likely than abstract, linguistic expressions to be successfully repressed from consciousness. Since memory can be coded into either verbal, logical or visual, analogical systems (Paivio, 1986), it has been postulated that cognitive performance increases with the imageability of material as items are more likely to be coded in both verbal and non-verbal modes (Marschark & Hunt, 1989). This would favour the use of imagery; in addition, it adheres to the main communicative imperatives of effective fear appeals: to be realistic, clear and simple in terms of the message, and to be thought provoking in nature and impact (Montazeri & McEwen, 1997).

Indeed, the better matched the fear stimuli are to the actual fear experienced (and smoking-related harm as opposed to exposure biomarker would seem to afford this), the more successful the treatment (e.g. see Mohlman & Zinbarg, 2000). Although findings support the claim that fear-evoking information may be transmitted in a variety of media, the relative efficacy of a particular medium in activating fear might depend on how well it can depict the elements of a given fear structure. The use of visual imagery may prove advantageous over purely verbal or numerical instructions in smoking fear appeals because it may not only increase a smoker's understanding of the smoking-disease link but it may also lead to a better evocation of relevant fear networks as indexed by increased physiological arousal (Vrana, Cuthbert, & Lang, 1986).

### **VII.iv.i Limitations**

This study has a number of limitations, which reduce the generalisability of findings. First, as already indicated, the sample was not randomly selected, which may have introduced systematic differences in comparison with the general population. Yet, demographic data (with possible exception of age) compared favourably to large-scale

epidemiological studies. Second, owing to a greater attrition than expected, the investigation was not powered enough to detect more subtle effects, which may have affected the evaluation of changes in cognitive antecedents of behaviour change and may have reduced the ability of this RCT to detect an overall effect of the intervention. Third, while it is assumed that the low-demand nature of this study minimised self-report bias on measures, this cannot be ruled out. Although biochemical outcome validation would have been desirable, it was not practically possible in this intervention.

Another problem relates to the quasi-experimental design that was used to assess the effectiveness of the leaflet in altering cognitive precursors of behaviour since this does not exclude the possibility that the findings were an artefact of the study. It is feasible that partaking in the study itself may have led to an increase in the cognitions assessed. However, this is unlikely since the laboratory study did not attempt to change perceptions and behaviour but rather the opposite: smokers were asked to continue smoking as normal over the 24 hours of the study period. Yet, the current study design does not allow delineating the impact of brief advice from the impact of the leaflet. However, the advice provided was very minimal indeed, and thus its influence on cognitive outcome variables likely to be small. Lastly, in order to better gauge the influence of EP, it would have been preferable to include more direct measures, such as blood pressure. As Foa and Kozak (1986) point out, people have an imperfect knowledge of the information contained in their fear networks, therefore physiological arousal would be particularly compelling evidence that their fear network had been activated.



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**VII.iv.ii Implications and conclusions**

In conclusion, this study provides evidence that offering a simple leaflet can change cognitive antecedents of behaviour change, and this effect can be enhanced through the provision of expired-air carbon-monoxide. Such biomarker feedback was shown to reduce perceptions of invulnerability (optimistic bias) regarding smoking-related illnesses, resulting in a greater motivation to stop smoking. However, findings suggest that these effects are short-lived and do not necessarily translate into action but rather are modified by perceptions of self-efficacy. This study could only provide partial confirmation for the causal interaction of the constructs of the EPPM and the predictions made by the EP model. Future research could include a larger sample to overcome power issues, have an additional intervention arm (minimal – no leaflet or feedback) to avoid confounding and use biologically-based measures to build on the findings from this study.

The fact that more people attempted to quit than sustained abstinence in this intervention emphasises the need to include appropriate relapse prevention measures in smoking interventions. Furthermore, the effect of self-efficacy on smoking cessation and motivation to stop highlights the need for successful smoking interventions to include techniques that can increase self-efficacy, such as proposed by Bandura (1994), in order to translate the momentum gained from these interventions into concrete behavioural outcomes. Exposure or susceptibility biomarker, however, may not be enough to instigate such behaviour change, especially in smokers that require more support and encouragement, and harm biomarkers, such as those described in the next two chapters, may prove generally more effective as an addendum to fear appeals.

## Chapter VIII

### **Study 4: An investigation of smoking and smoking cessation in people with diagnosed and undiagnosed chronic obstructive pulmonary disease<sup>50</sup>**

#### ***VIII.i Introduction***

Chronic obstructive pulmonary disease (COPD) is a syndrome denoting a largely irreversible obstruction of airflow composed in varying proportions of chronic bronchitis, bronchiolitis and emphysema (Lomas, 2002). COPD is a major contributor to global mortality and morbidity, and its worldwide prevalence is predicted to increase further (Murray & Lopez, 1997a). There are currently an estimated 900,000 people diagnosed with COPD in the UK (National Collaborating Centre for Chronic Conditions, 2004) and each year nearly 30,000 people die from the disease in England and Wales (Office for National Statistics, 2004). However, little is known about the true prevalence of COPD and estimates based on non-UK studies or UK studies with small samples suggest that this disease remains largely undiagnosed (Renwick & Connolly, 1996; Dickinson, Meaker, Searle, & Ratcliffe, 1999; Pena, Miravittles, Gabriel, Jimenez-Ruiz *et al.*, 2000; Mannino, Gagnon, Petty, & Lydick, 2000; Huchon, Vergnenegre, Neukirch, Bami *et al.*, 2002; Kim, Kim, Jung, Chang *et al.*, 2005).

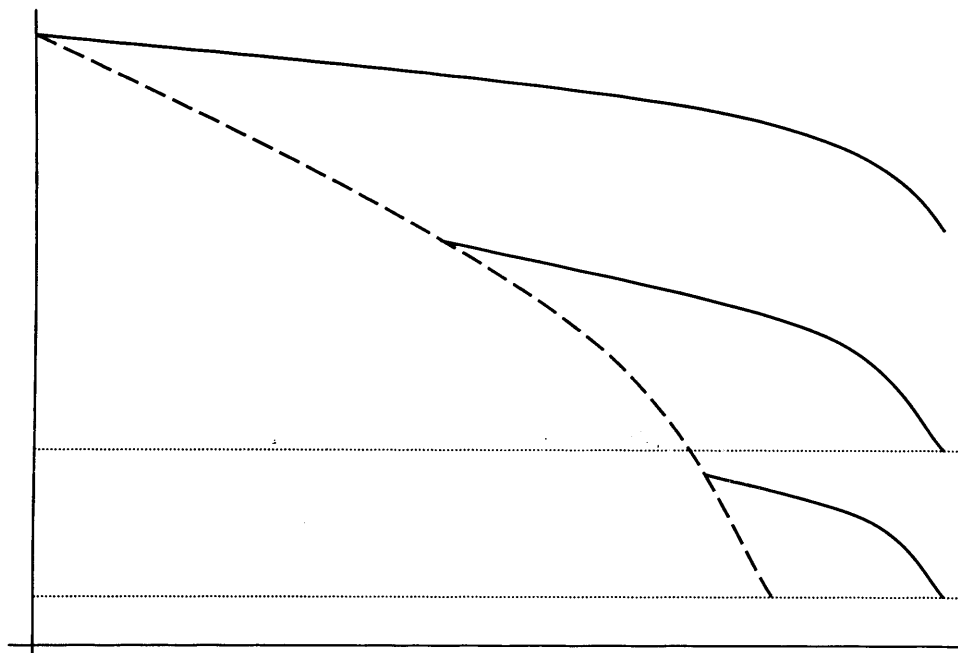
As highlighted in the introduction, it is well established that smoking is the single most important cause of COPD, increasing the risk of developing and dying from this condition by a factor of 13 (Doll, Peto, Wheatley, Gray *et al.*, 1994; Doll, 1999). Figure VIII.I shows the typical course of development of lung function over the lifespan among smokers and non-smokers. While never smokers and those not susceptible to smoke will

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<sup>50</sup> A version of this chapter and an associated research letter has been published (see Appendix VIII.I and Appendix VIII.II)

only experience a general decrease in lung function that is associated with ageing, susceptible smokers will have a rapid decline in their lung function in middle age, which will progress to cause premature disability and eventually death. However, smokers who stop are able to delay these effects and thus significantly prolong their lifespan (e.g. Floreani & Rennard, 1999; Wise, Kanner, Lindgren, Connett *et al.*, 2003).

**Figure VIII.I: Lung function decline by smoking status across lifespan^**



^Adapted from (Fletcher & Peto, 1977)

### VIII.i.i Rationale

Whereas the incidence of COPD in smokers, ex-smokers and never-smokers is well documented (Fletcher, Peto, Tinker, & Speizer, 1976; Lange, Groth, Nyboe, Mortensen *et al.*, 1989; Lundback, Lindberg, Lindstrom, Ronmark *et al.*, 2003; Kornmann, Beeh, Beier, Geis *et al.*, 2003), surprisingly little is known about the converse: the prevalence of smoking in people with COPD.

This is an important issue because it is vital to determine the scale of the problem of smoking in this vulnerable group, and the extent to which resources need to be put into

place to tackle it. Moreover, given that many people with COPD do not recognise that they have this condition (Calverley & Bellamy, 2000; van Schayck & Chavannes, 2003) and yet would benefit greatly from stopping smoking, it is crucial to identify the prevalence of undiagnosed COPD among smokers. As described above, it is known that smoking cessation is the most effective means of appreciably reducing the rate of disease progression and minimising acute exacerbations (van der Meer, Wagena, Ostelo, Jacobs *et al.*, 2003), but smokers need to be identified first before they can be helped to stop. Moreover, there is evidence that the identification of smokers with COPD may by itself increase motivation to stop and thus lead to increased smoking cessation rates (Czajkowska-Malinowska, Nowinski, Gorecka, & Zielinski, 2001). Beyond a simple diagnosis, the Lung Health Study has shown that with aggressive and prolonged intervention smokers with mild to moderate COPD can be helped to stop and that this has a beneficial effect on lung function and mortality (Kanner, Connett, Williams, & Buist, 1999; Anthonisen, Connett, & Murray, 2002).

Biological markers have played a crucial part in furthering our knowledge about the effects of smoking on health and possible causal disease mechanisms and the case of COPD is no exception. COPD can be defined and assessed using a variety of methods; however, there is currently no single diagnostic test that everyone is agreed on (National Collaborating Centre for Chronic Conditions, 2004). In fact, there exists some controversy regarding the best diagnostic procedure (Mannino, 2007). In general, COPD is defined on the basis of clinical judgement informed by patient history, physical examination and, crucially, confirmation of airflow obstruction using spirometry. Spirometry, and more specifically full vital capacity (FVC) and forced expiratory volume in one second (FEV<sub>1</sub>), which are computed from spirometric tests, provide a biological marker of the presence and severity of reduced lung function.

When people have lower lung elastic recoil because of the destruction of alveolar walls, as in emphysema, or show narrowing of the small airways owing to fibrosis, as in chronic bronchitis, this results in loss of both lung volume and airflow, which can be detected by spirometry (Rennard, 1998). Although other diagnostic tests exist, including whole body plethysmography to measure airways resistance or chest radiography to establish hyperinflation, spirometry is a favoured biological marker of COPD as it can be carried out easily, non-invasively and shows less variability than other forms of assessment (Siafakas, Vermeire, Pride, Paoletti *et al.*, 1995).

In addition to responses to survey questions, this study therefore used both spirometry, a biological marker of lung function, and saliva cotinine, a biomarker of tobacco smoking, to describe the prevalence and extent of under-detection of COPD, and associated smoking patterns, nicotine dependence and motivation to stop smoking in people with COPD. Data came from the Health Survey for England 2001 to examine these issues in a nationally representative sample.

### **VIII.i.ii    Aims**

Specifically, the aims of this chapter are:

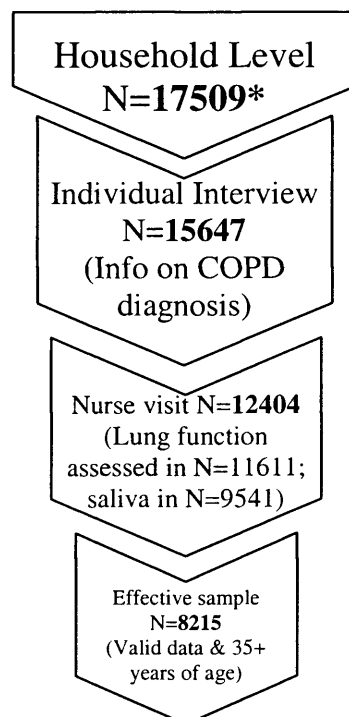
- 1) To describe prevalence and level of under-diagnosis of spirometry-defined COPD in this sample and among smokers and non-smokers.
- 2) To compare demographic characteristics, smoking prevalence and smoking patterns in people with and without spirometry-defined COPD adjusting for confounders.
- 3) To evaluate the association, if any, between receiving a diagnosis of a respiratory disease and motivation to stop smoking as well as smoking cessation.

## VIII.ii Methods

### VIII.ii.i Procedure and participants

The Health Survey for England (HSE) is an annual cross-sectional household survey that assesses the health of the population of England using a two stage process; an individual home interview, is followed by a visit from a nurse, who carries out a number of objective health assessments. The HSE in 2001 focused on asthma, respiratory conditions and disability, and included an assessment of lung function as well as the collection of saliva samples for cotinine assay. The methodology has been described in detail elsewhere (Prior, Deverill, Malbut, & Primatesta, 2003). Briefly, private households were identified with a multi-stage probability stratified sampling design<sup>51</sup> and its members invited to participate. Figure VIII.II provides a breakdown of the sample.

**Figure VIII.II: Flow-Chart Participants (16 yrs+)**



\*Estimate based on assumption of at least one adult in each eligible, non-responding household

<sup>51</sup> Postcode sectors, the primary sampling unit, were selected based on Census-derived stratification by geographical region and socio-economic group and included with a probability of selection proportional to its total number of addresses. Households at 19 addresses from each postcode sector were then systematically selected to be included in the survey.

Of eligible households, 74% (N=9373 households) agreed to take part in the 2001 survey. In co-operating households 15647 adults (89% response rate) were interviewed and 12404 adults (71% response rate) saw a nurse, who obtained lung function measures from 11611 and valid cotinine saliva samples from 9451 participants, which resulted in an effective sample of 8215 people above the age of 35 (74% of this population).

### **VIII.ii.ii Measures**

#### **VIII.ii.ii.i Demographic characteristics**

During the interview, data were collected on age, sex, and occupational status (by head of household). A deprivation score was computed from five measures (car ownership, educational attainment, housing tenure, employment status and occupation). Participants scored one for each of: no car; no qualifications; living in rented accommodation; being unemployed; and manual occupation. This gave a maximum deprivation score of five (Jarvis, Wardle, Waller, & Owen, 2003).

#### **VIII.ii.ii.ii Lung function**

Lung function was assessed by a trained nurse with a spirometer (Vitalograph Escort, Buckingham, UK) measuring forced expiratory volume in one second (FEV<sub>1</sub>), forced vital capacity (FVC) and peak expiratory flow (PEF). A total of 5 attempts were made and indicators of lung function obtained from the blow judged to be technically most satisfactory according to Health Survey guidelines were used in the analysis.

#### **VIII.ii.ii.iii Saliva cotinine**

Saliva samples were collected using a dental roll, which participants were asked to keep in the mouth until saturated. Samples were assayed for cotinine with a well established rapid gas liquid chromatography technique (Feyerabend & Russell, 1990). As previously indicated, cotinine is a major metabolite of nicotine that provides an extremely sensitive and specific quantitative measurement of smoking; in the absence of

the use of nicotine replacement products saliva cotinine concentrations above 15 ng/ml usually indicate personal tobacco use (Jarvis, Tunstall-Pedoe *et al.*, 1987).

### **VIII.ii.ii.iv Smoking characteristics**

Cigarette smoking status was assessed by self-report and saliva cotinine analysis.

Participants classified themselves as current cigarette smokers, ex-smokers or non-smokers. Participants also reported how long they had been smoking for and, if applicable, how long ago they had stopped smoking. Cotinine concentrations over 15 ng/ml in self-reported ex-or non-smokers who did not indicate use of nicotine replacement therapy were taken to imply personal tobacco use, i.e. current smoking.

Cigarette dependence was estimated by the Heaviness of Smoking Index (HSI) (Heatherton, Kozlowski *et al.*, 1989) a short version of the Fagerström test for nicotine dependence. The HSI is calculated from the time to the first cigarette (4 categories, 0-3) and cigarettes per day (4 categories, 0-3) producing a scale from 0 to 6 with higher scores indicating greater nicotine dependence. Motivation to stop smoking was assessed by a single questionnaire item that asked smokers whether they would like to give up smoking altogether (yes/no).

### **VIII.ii.ii.v Respiratory disease**

#### *Objective assessment:*

Measures from the lung function test were used to determine COPD according to joint American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines (Celli & MacNee, 2004), also called GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria. COPD is defined as a  $FEV_1/FVC$  ratio below 0.7. In the presence of this obstruction,  $FEV_1$  above 80% of predicted value is categorised as mild,  $FEV_1$  between 50 and 79% of predicted value as moderate,  $FEV_1$  between 30 and 49% of predicted value as severe and  $FEV_1$  below 30% of predicted value as very severe COPD. Since numbers in these latter two groups were small, we combined them for the



purpose of this analysis. Predicted values are based on age, sex and height adjusted expected population reference norms for lung function measurements (Quanjer, Tammeling, Cotes, Pedersen *et al.*, 1993).

As described in the introduction, some controversy exists regarding the suitability of existing criteria for the definition of COPD in general and the GOLD definition in particular, since it relies on a fixed cut-off point that is, in fact, dependent on age. It has been suggested that GOLD will therefore lead to a substantial under-diagnosis of obstructive lung disease in younger people and an over-diagnosis of COPD in older individuals (e.g. Hnizdo, Glindmeyer, Petsonk, Enright *et al.*, 2006). In order to overcome this possible bias, some of the analyses were repeated using the LLN (lower level of normal) method, which relies on age-dependent norms that are based on the lung function in the bottom 5% of the healthy population (non-smokers with no reported respiratory symptoms) to provide cut-off points for a COPD diagnosis. Reference values for this analysis were taken from a previous study (Falaschetti, Laiho, Primatesta, & Purdon, 2004). In general, however, unless it is otherwise stated, spirometry-defined COPD data reported in this chapter are determined with GOLD criteria as this is the more commonly used measure.

### *Self-report:*

During the interview respondents were asked if they had any long-standing illness or disability. If they responded yes, they were asked what the condition was and up to six different infirmities were recorded. Respiratory diseases were coded as 'chronic bronchitis and/or emphysema', 'asthma' or 'other respiratory complaints'. If participants volunteered that they had any of these conditions, they were considered to have been diagnosed. We defined COPD as 'undiagnosed' if participants with spirometry-defined COPD did not report having any of the above conditions.

### **VIII.ii.iii Contributors**

The Health Survey for England is commissioned by the Department of Health and carried out by the Joint Survey Unit of the National Centre for Social Research and the Department of Epidemiology and Public Health, University College London. The data were made available through the UK Data Archive. These bodies bear no responsibility for the analyses and interpretation of this Chapter. Robert West and myself conceived and devised this analysis. Martin Jarvis, Robert West and myself analysed the data and John Britton, Martin Jarvis, Robert West and myself contributed to the interpretation of the data and I wrote up this Chapter.

### **VIII.ii.iv Statistical Analysis**

Data were not weighted in adults as comparison with the 2001 Census indicated that the sample was sufficiently representative of the population (Prior, Deverili *et al.*, 2003). Since COPD is a disease which is rarely diagnosed in young adults (Doherty & Briggs, Jr., 2004), all the analyses were restricted to people above 35 years of age. Data were analysed using SPSS 13.0 and STATA 9.0. Parametric assumptions for continuous variables were examined by looking at histograms as well as the skewness and kurtosis of data<sup>52</sup> to assess normality of distribution and Levene's test to assess homogeneity of variance. Where variables failed assumptions, appropriate non-parametric tests were carried out. Group differences for and adjustments of continuous variables were analysed by univariate ANOVA followed by Tukey HSD post-hoc test to determine which group differences, if any, were reliable. Chi-square tests were carried out to investigate between group differences for categorical and dichotomous variables; adjustments in proportions were compared with Mantel-Haenszel test and calculated by the direct standardisation method using the total study population as the standard. Where appropriate, partial correlation and logistic regression analyses were conducted

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<sup>52</sup> Values between -1 and 1 were considered normal

to evaluate associations between variables and to estimate odds ratios. Since this study used stratified, clustered sampling and to account for multiple comparisons significance values were adjusted using the false discovery rate control (Benjamini & Hochberg, 1995).

### VIII.iii Results

#### VIII.iii.i The prevalence and diagnosis of COPD

From a total of 15467 respondents, 11101 were aged over 35 years of whom 8215 had valid spirometry data. Those excluded due to missing spirometry data did not differ on any smoking characteristic; however, they were more likely to be manual workers, older, female and deprived. Spirometry-defined COPD as defined by GOLD criteria was present in 1093 individuals (13.3%, 95%CI 12.6 to 14.0% of respondents, see Table VIII.I). Prevalence was somewhat lower at 11.2 % (95%CI 10.5-11.9) when using the LLN method. According to GOLD cut-off points, moderate COPD was found in 5.8%, followed by mild (5.5%) and severe or very severe COPD (1.9%).

**Table VIII.I: Spirometry-defined COPD GOLD prevalence by smoking status**

	Total N=8215		Never Smokers N=3685		Ex-Smokers N=2551		Smokers N=1978	
COPD	Percent (N)							
Mild	5.5	(455)	4.9	(180) <sup>a</sup>	5.5	(141) <sup>a,b</sup>	6.8	(134) <sup>b</sup>
Moderate	5.8	(480)	3.1	(116) <sup>a</sup>	7.1	(180) <sup>b</sup>	9.3	(184) <sup>c</sup>
Severe or very severe	1.9	(158)	0.7	(26) <sup>a</sup>	2.7	(68) <sup>b</sup>	3.2	(64) <sup>b</sup>
Overall	13.3	(1093)	8.7	(322) <sup>a</sup>	15.2	(389) <sup>b</sup>	19.3	(382) <sup>c</sup>

<sup>a,b,c</sup> Different letters indicate significant group differences (p<0.025)

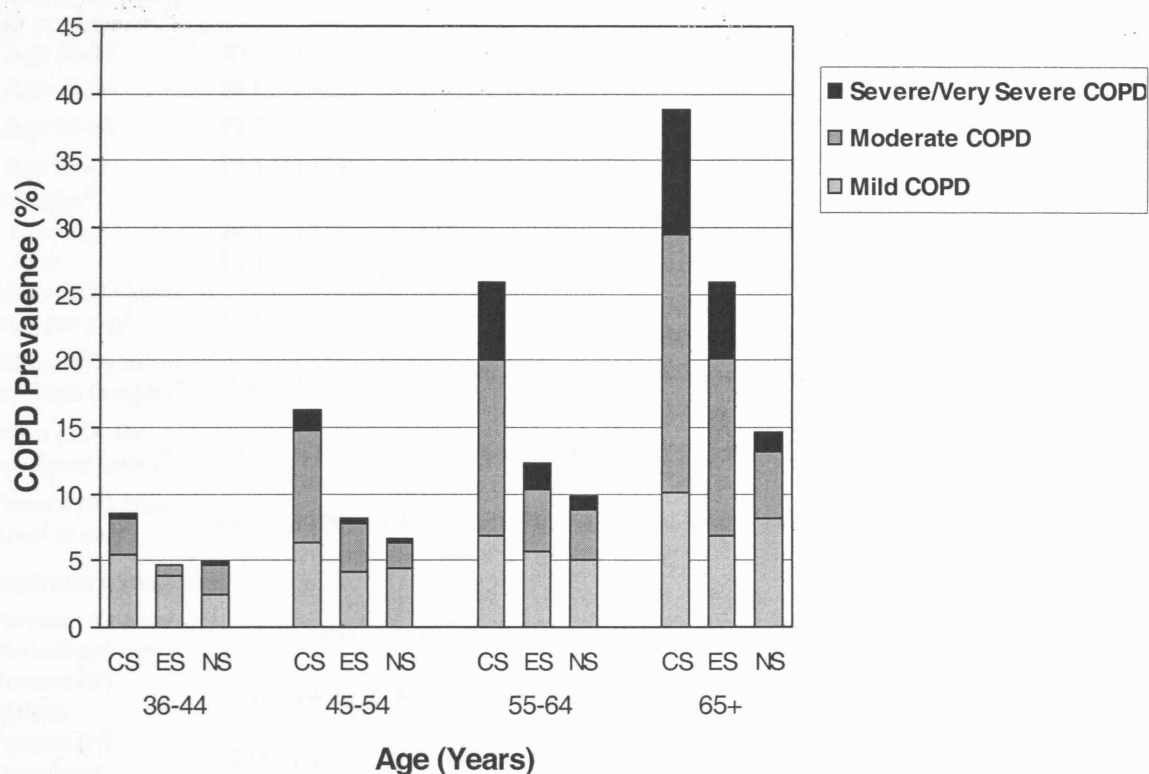
As would be expected, COPD was most common among current smokers (19.3%) followed by ex-smokers (15.2%) and never smokers (8.2%). These differences were significant between all groups, and the gap in COPD prevalence between current or ex-smokers and never smokers increased in relation to disease severity (see Table VIII.I).

Although the absolute number of COPD cases was nearly equal for never and former or current smokers, this was primarily due to a larger number of mild cases among never smokers.

Table VIII. General descriptive statistics of GOLD status

Figure VIII.III shows an approximately linear increase in COPD prevalence with age irrespective of smoking status. However, this increase was steeper among current and ex-smokers, so that almost half of smokers above 65 years of age had some lung function impairment compared but only 15% of never smokers. In addition, moderate and severe or very severe COPD was more prevalent and also occurred earlier in current and former smokers, while even in the oldest age group only a very small proportion of never smokers had developed the most acute form of COPD.

**Figure VIII.III: GOLD COPD status stratified by age and smoking status**



CS= Current Smokers, ES= Ex-smokers, NS = Never Smokers

Just 18.8% (95%CI 16.4 to 21.1) of those with spirometry-defined COPD by GOLD criteria reported having been diagnosed with a respiratory disease of any kind (see Table VIII.II).

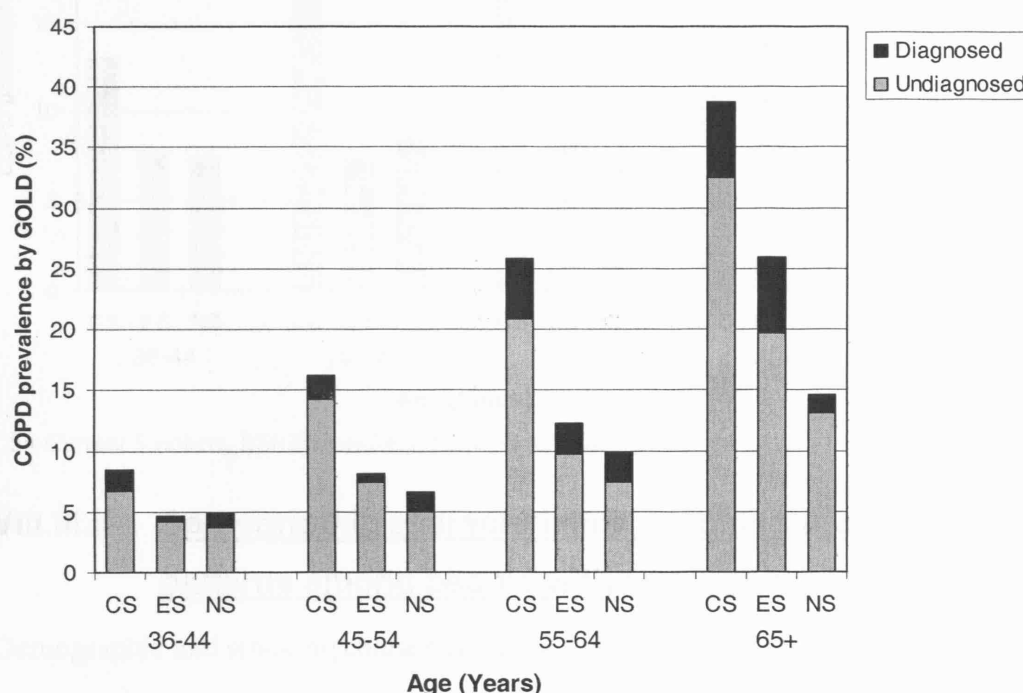
**Table VIII.II: General descriptives by spirometry defined COPD and COPD gradation using GOLD criteria**

	Total Sample N=8215		No COPD N=7122		COPD N=1093		COPD Gradation					
							Mild N=455		Moderate N=480		Severe/v. severe N=158	
Demographics												
Mean (SD) Age	55.5	(13.5)	54.4	(13.2)	62.5	(13.4)***	60.2	(14.2) <sup>a</sup>	63.0	(13.0) <sup>a</sup>	67.2	(10.8) <sup>b</sup>
Percent (N) Male	46.4	(3808)	44.7	(3185)	57.0	(623)***	50.8	(231) <sup>a</sup>	61.9	(297) <sup>b</sup>	60.1	(95) <sup>a,b</sup>
Percent (N) Manual work	44.6	(3664)	43.6	(3105)	51.1	(559)***	44.6	(203) <sup>a</sup>	55.6	(267) <sup>b</sup>	56.3	(89) <sup>b</sup>
Mean (SD) Deprivation score <sup>§</sup>	1.1	(1.2)	1.1	(1.1)	1.3	(1.2)***	1.2	(1.2) <sup>a</sup>	1.7	(1.2) <sup>b</sup>	1.8	(1.2) <sup>b</sup>
Smoking												
Percent (N) Smoking prevalence												
Age 36-44	30.4	(654)	29.6	(599)	43.3	(55)**	45.5	(35) <sup>a</sup>	40.0	(18) <sup>a</sup>	40.0	(2) <sup>a</sup>
Age 45-54	28.8	(610)	26.7	(511)	47.8	(99)***	37.5	(39) <sup>a</sup>	57.3	(51) <sup>b</sup>	64.3	(9) <sup>a,b</sup>
Age 55-64	22.0	(379)	19.1	(281)	40.0	(98)***	26.5	(26) <sup>a</sup>	47.2	(50) <sup>b</sup>	53.7	(22) <sup>b</sup>
Age 65+	15.1	(335)	12.0	(205)	25.3	(130)***	19.3	(34) <sup>a</sup>	27.1	(65) <sup>a,b</sup>	31.6	(31) <sup>b</sup>
All ages <sup>¶</sup>												
Current	24.1	(1978)	22.4	(1596)	34.9	(382)***	29.5	(134) <sup>a</sup>	38.3	(184) <sup>b</sup>	40.5	(64) <sup>b</sup>
Ever	55.1	(4529)	52.8	(3758)	70.5	(771)***	60.4	(275) <sup>a</sup>	75.8	(364) <sup>b</sup>	83.5	(132) <sup>b</sup>
Mean (SD) Cigarettes per day <sup>#</sup>	15.1	(9.5)	14.8	(9.2)	16.3	(10.4)*	16.3	(9.2) <sup>a</sup>	17.1	(11.6) <sup>a</sup>	13.9	(8.5) <sup>a</sup>
Mean (SD) saliva cotinine in ng/ml <sup>#</sup>	286	(177)	278	(177)	322	(173)***	306	(171) <sup>a</sup>	336	(169) <sup>a</sup>	318	(192) <sup>a</sup>
Mean (SD) Dependence rating <sup>¶</sup>	3.7	(1.0)	3.6	(1.0)	3.9	(1.0)***	3.9	(1.0) <sup>a</sup>	3.8	(0.9) <sup>a</sup>	3.6	(1.0) <sup>a</sup>
Percent (N) Motivated to quit <sup>‡</sup>	68.9	(1200)	68.0	(955)	70.8	(239)	65.2	(76) <sup>a</sup>	77.3	(126) <sup>a</sup>	61.8	(37) <sup>a</sup>
Respiratory Diagnosis												
Percent (N) Bronchitis/Emphysema	1.1	(89)	0.7	(52)	3.4	(37)***	0.4	(2) <sup>a</sup>	3.3	(16) <sup>b</sup>	12.0	(19) <sup>c</sup>
Percent (N) Asthma	5.6	(456)	4.5	(319)	12.5	(137)***	5.1	(23) <sup>a</sup>	14.0	(67) <sup>b</sup>	29.7	(47) <sup>c</sup>
Percent (N) Undefined	2.0	(164)	1.7	(123)	3.8	(41)***	0.9	(4) <sup>a</sup>	5.0	(24) <sup>b</sup>	8.2	(13) <sup>b</sup>
Percent (N) Any	8.2	(671)	6.5	(466)	18.8	(205)***	6.4	(29) <sup>a</sup>	21.3	(102) <sup>b</sup>	46.8	(74) <sup>c</sup>

\*Excluding non-smokers, <sup>§</sup> Adjusted for age, <sup>‡</sup> Adjusted for age and sex, <sup>¶</sup> Adjusted for age, sex and deprivation level, \*\*\*p<0.001, \*\*p<0.01, \*p<0.025; <sup>a,b,c</sup> Different letters indicate significant group differences (p<0.025)

The level of diagnosis (and thus the degree of under-detection) was similar to that determined by the LLN method (21.2%; 95%CI 18.5-23.9). Thus in adults above 35 years of age there were over 4 undiagnosed cases of spirometry-defined COPD for every case reporting any respiratory disease. The extent of this under-diagnosis decreased significantly in relation to disease severity, but even among those with severe or very severe COPD, less than half reported a respiratory diagnosis (Table VIII.II).

**Figure VIII.IV: GOLD COPD prevalence and diagnosis stratified by age and smoking status**

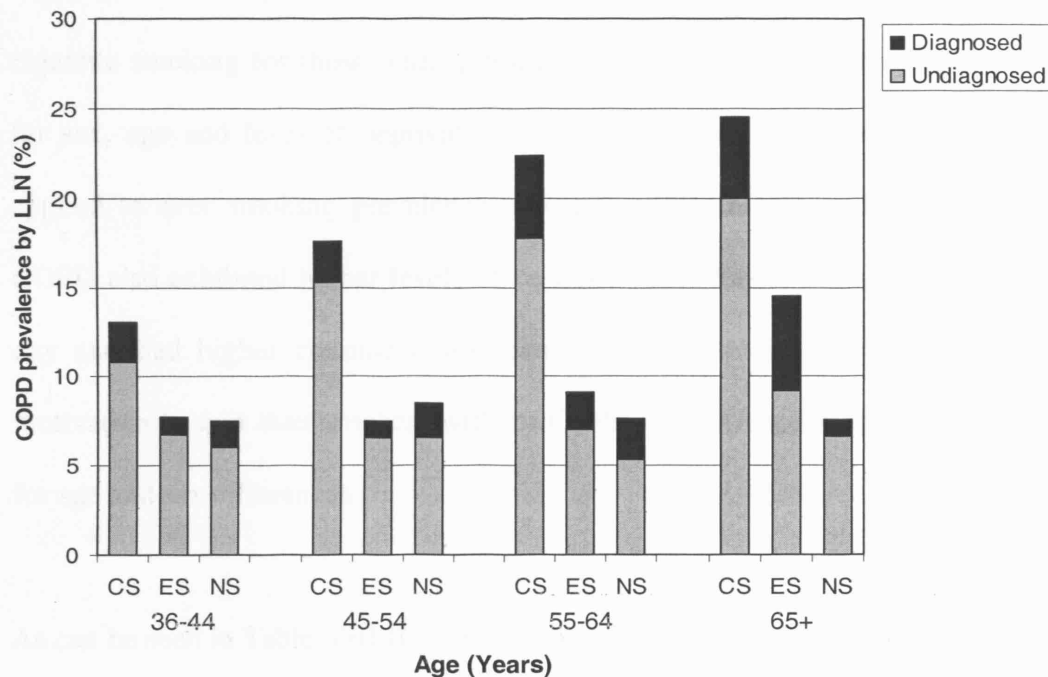


As can be seen in Figure VIII.IV, when stratifying diagnosis by age and sex, irrespective of smoking status there was no apparent change in the level of diagnosis as people got older ( $\chi^2(3)=2.73$ ,  $p=0.44$ ). Moreover, looking across ages at the total population above 35 years of age, it seems that smokers were not more likely to be diagnosed with COPD than either ex-smokers or never smokers ( $\chi^2(1)=1.98$ ,  $p=0.16$ ).

As expected, using the LLN method to define COPD led to more people in the younger and fewer people in the older age-range being classified as having COPD compared with GOLD criteria (see Figure VIII.V). However, it is obvious the LLN method

provides very similar results in terms of the level of diagnosis. COPD was highly under-diagnosed in all age groups irrespective of the smoking status.

**Figure VIII.V: LLN COPD prevalence and diagnosis stratified by age and smoking status**



CS= Current Smokers, ES= Ex-smokers, NS = Never Smokers

#### **VIII.iii.ii Demographic characteristics, smoking prevalence and patterns among people with and without COPD**

Demographic and smoking characteristics of this sample are provided in Table VIII.II.

People with spirometry-defined COPD were more likely to be older, manual workers, male, and socio-economically deprived than those without the disease, and increasingly so in relation to disease severity. They were also more likely to be diagnosed with a respiratory disease of any kind than people without COPD. Similarly, the more severe the disease, the more likely people were to volunteer a diagnosis with chronic bronchitis/emphysema, asthma or any other respiratory disease.

A significantly larger proportion of people of all ages with spirometry-defined COPD reported having ever been a smoker than respondents without COPD (Table VIII.II).

Current cigarette smoking was also significantly higher among people with COPD (34.9%, 95%CI 32.1 to 37.8) than among people without COPD (22.4%, 95%CI 21.4 to 23.4); cigarette smoking prevalence was even higher when using the LLN method to determine COPD (39.5%; 95%CI 36.3-42.7). The increased likelihood of current cigarette smoking for those with spirometry-defined COPD remained after adjustment for sex, age and level of deprivation (OR 2.25, 95%CI 1.94 to 2.62) and the same applied to ever smoking prevalence (OR 1.86, 95%CI 1.61 to 2.14). Smokers with COPD also exhibited higher levels of cigarette dependence, smoked more cigarettes a day and had higher cotinine concentrations. However, they did not display higher motivation to quit than smokers without COPD; this effect remained after adjustment for age and sex differences.

As can be seen in Table VIII.II, there was a graded association between severity of lung function impairment and current cigarette smoking and ever-smoking; greater impairment was associated with both higher cigarette and higher ever-smoking prevalence even when controlling for age, sex and deprivation level ( $\beta=0.445$ ,  $p<0.001$  and  $\beta=0.398$ ,  $p<0.001$ , respectively). While the majority of people with mild spirometry-defined COPD were former or never smokers (70.5%), this proportion decreased to 59.5% in people with severe or very severe COPD. Differences in current smoking were significant between those with mild and those with moderate or severe/very severe COPD (Table VIII.II).

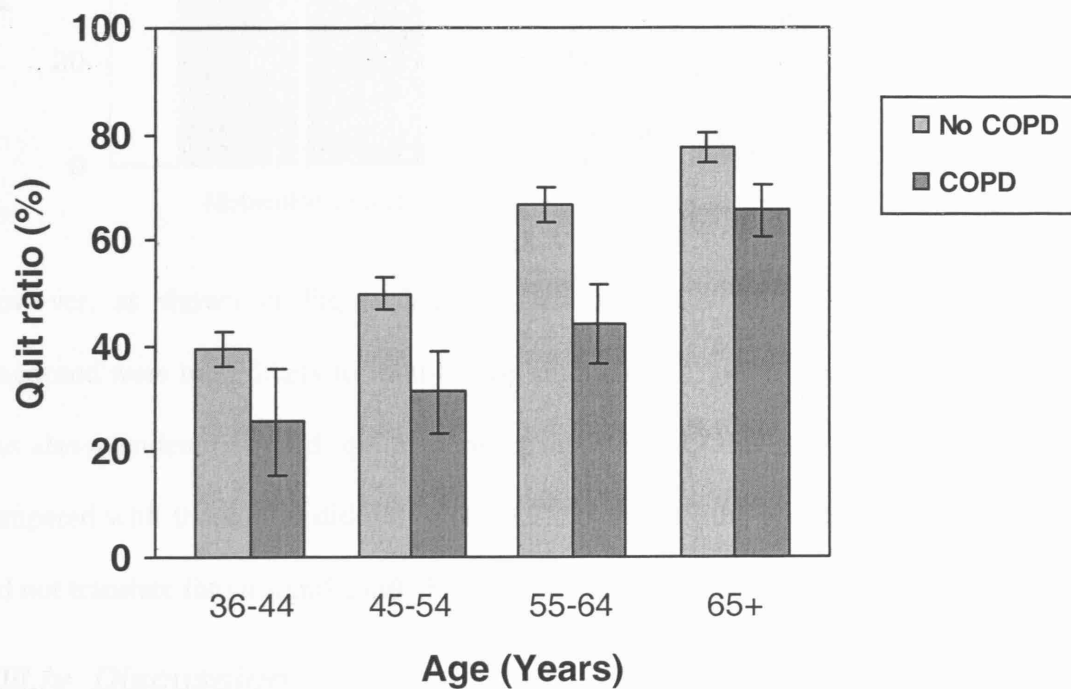
Self-reported smoking status was compared with cotinine-validated smoking status in order to estimate misreporting of current smoking in this sample. Among adults of all ages with spirometry-defined COPD, a significantly higher proportion of self-reported non-current smokers were actually smokers (5.2 %) than among people with normal



lung function (3.0%; OR 1.8, 95%CI 1.2 to 2.5). The majority of misreporting was accounted for by smokers claiming to be ex-smokers rather than never-smokers.

Figure VIII.VI highlights changes in smoking cessation behaviour over time among people with and without COPD by looking at the quit ratio. The quit ratio represents the proportion of people who have given up smoking out of the total of people who reported having ever smoked regularly within each year group and thus excludes the population of never smokers. This figure shows that there was a trend towards smoking cessation over time irrespective of COPD status; an increase in age was associated with an increase in the quit ratio.

**Figure VIII.VI: Quit-ratio; ex-smokers as proportion of ever-smokers by age group and GOLD COPD status**

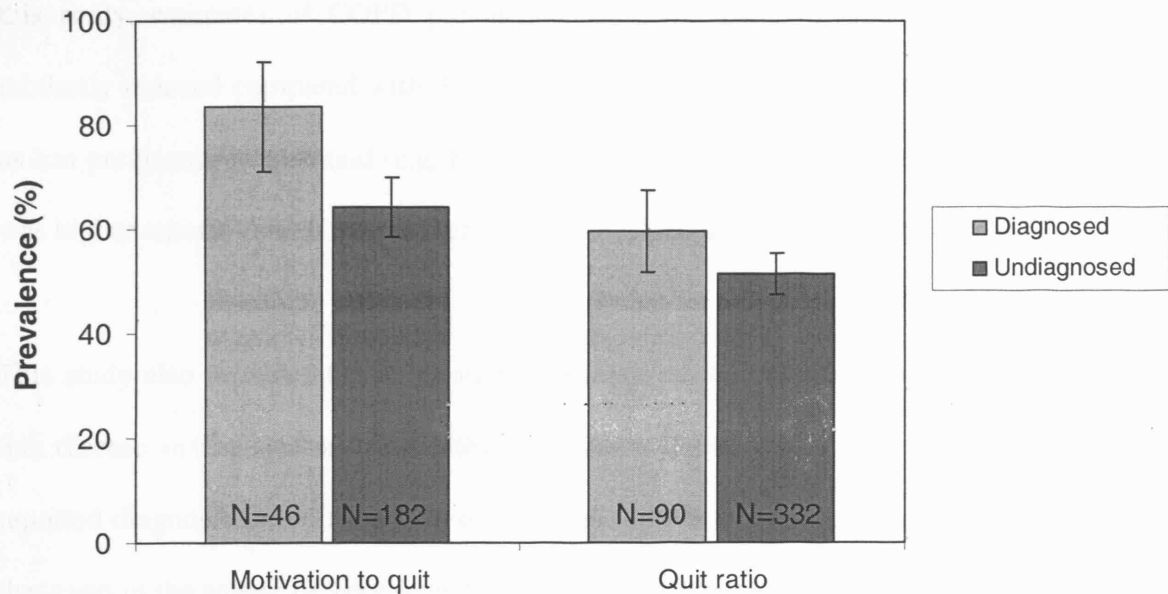


However, within each age group the quit ratio was considerably lower for people with than without COPD. Smokers who already have spirometry-defined COPD were much more likely to continue smoking and much less likely to give up smoking as they grow older compared with smokers without COPD.

### VIII.iii.iii Impact of diagnosis on motivation to stop and smoking cessation

Among people who had COPD by spirometry, there were no differences on any of the assessed socio-demographic variables between those who had and those who had not reported a diagnosis with any respiratory disease.

**Figure VIII.VII: Motivation to quit and quit-ratio by diagnosis among people with COPD by GOLD criteria**



However, as shown in Figure VIII.VII, smokers with the disease who had been diagnosed were more likely to want to stop smoking ( $\chi^2(1)=7.83$ ,  $p=0.005$ ). While there was also a tendency towards quitting among those with COPD who reported a diagnosis compared with those who did not ( $\chi^2(1)=3.25$ ,  $p=0.072$ ), the greater motivation to stop did not translate into a significantly higher quit ratio in this sample.

### VIII.iv *Discussion*

This study provides the first large-scale estimate of spirometrically defined COPD in England and one of very few estimates using objective diagnostic measures in a nationally representative population sample from any country in the world (Halbert, Isonaka, George, & Iqbal, 2003). The results are broadly comparable to previous COPD prevalence estimates employing spirometry testing and higher prevalence figures

reported in some (Kim, Kim *et al.*, 2005) but not other studies (Pena, Miravittles *et al.*, 2000; Mannino, Gagnon *et al.*, 2000) are probably due to differences in the age groups tested. Indeed, prevalence estimates vary widely in published studies with estimates as low as 0.23% and as high as 18.3%, which probably reflects not only differences in risk exposure or characteristics of the population sampled but also the variety of methods and definitions used to determine COPD by spirometry (Halbert, Isonaka *et al.*, 2003). In this study, estimates of COPD prevalence using the LLN method were only very modestly reduced compared with the GOLD standard figures for prevalence; however, as has previously been found (e.g. Falaschetti, Laiho *et al.*, 2004), prevalence by LLN was higher among younger and lower among older people compared with GOLD.

This study also provides the first national estimate of the extent of under-diagnosis of this disease in England and indicates that even with an inclusive definition of self-reported diagnosis, more than 80% of all cases did not report a clinical diagnosis, and that even in the severe or very severe category only 50% appear to have been clinically diagnosed. Again, using the LLN method only slightly reduced these estimates and produced broadly comparable figures underlining that under-diagnosis of COPD is a serious problem irrespective of the method used to objectively assess COPD. Interestingly, stratification by age and smoking status showed that COPD is not more likely to be picked up in relative (though it is in absolute) numbers as people grow older or among smokers compared with ex- or never smokers. This finding is surprising considering that older people are more likely to be seen by a health professional (Campbell & Roland, 1996) and that current smoking is part of the clinical diagnosis of COPD (e.g. Celli & MacNee, 2004), both of which would suggest that older people and smokers should be more likely to be diagnosed.

As would be expected, while the majority of people with COPD were former or never smokers, the prevalence of current cigarette smoking in people with spirometry-defined COPD was higher than in the general population and this is the first study to provide an estimate of that prevalence. It was found that almost half of those with spirometry-defined COPD smoked in middle age and that across all ages smokers with COPD were less likely to quit than those without impaired lung function. They also tended to be more cigarette dependent than those without COPD, but not more motivated to stop.

However, results also suggest that a diagnosis with COPD may increase motivation to stop smoking as shown by a larger proportion of smokers with objective signs of COPD wanting to stop when they also reported a diagnosis with a respiratory disease. Indeed, as outlined in the introductory chapters, there is some evidence that feedback of spirometry results together with brief advice may increase motivation and even cessation in this population (e.g. Humerfelt, Eide, Kvale, Aaro *et al.*, 1998; Gorecka, Bednarek, Nowinski, Puscinska *et al.*, 2003). Yet, in the current study there was no evidence of an impact of a diagnosis on actual cessation rates and this is in line with most studies that have looked at this issue (Badgett & Tanaka, 1997).

### **VIII.iv.i Limitations**

This study has a number of limitations that need to be kept in mind when evaluating the results. First, as data came from a cross-sectional survey, the analysis does not allow for conclusions regarding causal associations to be drawn. Yet, since the Health Survey for England is a large, nationally representative, well-designed and methodologically rigorous investigation, and considering the lack of commensurate longitudinal surveys, the analysis in this cross-sectional study can, at a minimum, provide some preliminary evidence and suggestions for possible causal pathways. Second, the assessment of COPD was based on spirometry alone and did not involve reversibility testing to

exclude asthma. Since the sample included participants below 45 years of age, when asthma may be more probable than COPD, this may have resulted in an overestimation of COPD prevalence. However, there is considerable controversy regarding the use of reversibility testing to identify COPD as response to testing can be variable and therefore misleading (Calverley, Burge, Spencer, Anderson *et al.*, 2003). Moreover, the overlap between irreversible airway obstruction and chronic (obstructive) asthma is generally acknowledged, the latter being included in the ICD 10 definition of COPD. In addition, analyses were repeated using a different method not dependent on bronchodilator testing, which yielded very similar results. The use of spirometric assessment alone to estimate COPD prevalence in a large sample above 35 years of age would therefore seem justified. Third, as people who did not participate in spirometry testing differed on a number of demographic characteristics, this may have biased results leading to an underestimation of COPD prevalence. However, as the results were comparable to previous studies, this bias, if present, did not have a large effect on prevalence rates. Lastly, only self-report data were available in order to determine whether a respiratory condition had been detected previously. While recall bias may have affected the reliability of reported conditions, this would have been counteracted by the liberal definition of 'diagnosed' COPD, which included other respiratory disorders.

### **VIII.iv.ii Implications and conclusions**

These results have implications for the recognition, prevention and treatment of COPD in primary and secondary care. Increasing awareness of COPD in the general population and specifically among smokers would aid the early diagnosis of this disease. The high level of smoking among people with spirometry-defined COPD and unreliability of self-reported smoking status among smokers with COPD underlines the necessity for the objective assessment of smoking status in chest clinics. In primary care, there is a need

to identify middle-aged smokers with undiagnosed COPD. While many would be mild or moderate cases, these smokers would also experience the greatest personal health gain from quitting (Pride, 2001) and are therefore a particularly strong priority group for intervention (Wilson, Adams *et al.*, 2005). Based on estimates of lung function decline in smokers and non-smokers (James, Palmer, Kicic, Maxwell *et al.*, 2005), one in every three current smokers with mild or moderate COPD in this sample who would go on to develop severe or very severe COPD over the next five years could avoid this disease progression if they stopped smoking.

The societal economic burden of COPD far outweighs the cost of routine spirometric assessment of at-risk smokers in primary care (Calverley & Bellamy, 2000; van Schayck & Chavannes, 2003; Britton, 2003). However, as shown in this analysis, while a diagnosis with a respiratory disease increases motivation, it is not enough; high levels of nicotine dependence among people with COPD militate against the effectiveness of spirometry feedback and brief smoking counselling alone to raise cessation rates. Interventions aimed at middle aged smokers with COPD need to be more intensive in order to increase their desire to stop further and address the greater level of addiction in this group. As has been shown by the Lung Health Study (Kanner, Connett *et al.*, 1999; Anthonisen, Connett *et al.*, 2002) aggressive and prolonged smoking cessation treatment can make a real difference in terms of lung function decline and mortality from COPD. Although it is unlikely that the duration and intensity of support that was given in the Lung Health Study would be offered to smokers more generally, the imperative to achieve cessation as soon as possible is so great in this group that arguably they may be considered a special case.

## Chapter IX

### **Study 5: An investigation of smoking and smoking cessation in people with diagnosed or undiagnosed cardiovascular disease and cardiovascular disease risk factors<sup>53</sup>**

#### ***IX.i Introduction***

Cardiovascular diseases present not only the most common cause of death in the UK - in 2005 over 180000 people in England and Wales died because of a disease of the circulatory system, nearly half from ischemic heart disease (Office for National Statistics, 2006) – but they are also the biggest contributors to global mortality and morbidity (Murray & Lopez, 1997b). As outlined in Chapters I and II, smoking has important consequences for the development and progression of cardiovascular diseases such as angina pectoris or myocardial infarction (e.g. see Lakier, 1992; Chen & Boreham, 2002; Burns, 2003). Although there is some debate about the precise mechanism through which smoking causes CVD, it is likely that smoking primarily increases the risk of heart disease through its involvement in the pathogenesis of thrombosis and atherosclerosis (e.g. Pech-Amsellem, Myara, Storogenko, Demuth *et al.*, 1996). Smoking causes arterial endothelial cell damage and increases plasma cholesterol and low-density lipoproteins, while decreasing high-density lipoproteins (e.g. Brischetto, Connor *et al.*, 1983), which leads to the development of plaque. It increases platelet stickiness, reactivity and sympathetic tone (Sleight, 1993) and may also influence the cellular immune system and promote aberrant expression of DNA resulting in cellular hyperplasia (Barrett & Benditt, 1988). In addition, smoking affects plasma coagulation pathways and a number of other factors involved in the progression of atherosclerosis (Diana, 1990) and thrombosis (Bottcher & Falk, 1999).

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<sup>53</sup> Analyses from this chapter have been presented as a poster (see Appendix IX.I)

Some studies have estimated that as many as 40% of CVD cases in Western countries are due to smoking compared with 31% due to high blood pressure and 24% due to cholesterol (Isles, Hole, Hawthorne, & Lever, 1992). Fortunately, many of the smoking-related effects on the cardiovascular system are reversible as shown by reduced CVD mortality after smoking cessation among either initially healthy individuals (e.g. Ben-Shlomo, Smith, Shipley, & Marmot, 1994) or cardiac patients (e.g. Hermanson, Omenn, Kronmal, & Gersh, 1988). Indeed, stopping smoking may halve the risk of subsequent CVD-related events (Wilhelmsson, Vedin, Elmfeldt, Tibblin *et al.*, 1975) while modulation of other risk factors may decrease risk by between maximally 35% (for cholesterol lowering therapy; 4S Study, 1994) and 30% (for blood pressure reduction; Collins, Peto, MacMahon, Hebert *et al.*, 1990). Moreover, some research suggests that stopping smoking can reduce the risk of heart attacks even to that of never smokers (e.g. Dobson, Alexander, Heller, & Lloyd, 1991).

Although – as shown in Table IX.I – there are many other modifiable and pertinent lifestyle risk factors for CVD such as exercise, obesity, alcohol consumption (e.g. Poulter, Sever, & Thom, 1993) and low fruit or vegetable consumption (Ness & Powles, 1997), it is clear that smoking cessation is of utmost importance for both the primary and secondary prevention of cardiovascular diseases. For this reason, the need for doctors to advise patients to stop smoking is amply stressed in various guidelines on CVD prevention (e.g. Ockene & Miller, 1997; Wood, De Backer G., Faergeman, Graham *et al.*, 1998; Pearson, Blair, Daniels, Eckel *et al.*, 2002; Wood, Durrington, McInnes, Poulter *et al.*, 2005; Smith, Jr., Allen, Blair, Bonow *et al.*, 2006). Moreover, determining smoking status as well as offering quit smoking advice have both been



included among the quality of care indicators for CVD within the Quality and Outcomes Framework (QOF)<sup>54</sup> introduced in the UK in 2004 (Department of Health, 2004).

**Table IX.I CVD risk factors**

Major independent risk factors
Smoking
Elevated blood pressure
Elevated serum total (and LDL <sup>¶</sup> ) cholesterol
Low serum HDL <sup>¶</sup> cholesterol
Diabetes mellitus
Advancing age
(Central) obesity <sup>‡</sup>
Physical inactivity <sup>‡</sup>
Excessive alcohol consumption <sup>‡</sup>
Predisposing risk factors*
Family history of premature CVD
Ethnic characteristics
Psychosocial characteristics
Conditional risk factors <sup>~</sup>
Elevated serum triglycerides / lipoprotein(a) / homocysteine
Prothrombotic factors (e.g. fibrinogen)
Inflammatory markers (e.g. C-reactive protein)

<sup>¶</sup>HDL/LDL: high-/low-density lipoprotein; <sup>‡</sup>Independent contribution debated;

\*Increase in CVD risk but causative, independent and quantitative contribution not well documented; <sup>~</sup>Worsen independent risk factors

### **IX.i.i Rationale**

While the prevalence of CVD and associated risk factors in smokers is well documented very little is known about the converse – the smoking prevalence among people with CVD and related risk factors. This is important for both primary and secondary prevention of cardiovascular morbidity and mortality. Determining the rate of smoking among people who are either likely to develop CVD (i.e. among those displaying a range of risk factors) or have already developed CVD is crucial in order to identify both the scale of this problem and the level of resources that need to be put into place to aid the prevention of CVD-related deaths in smokers. In addition, it is essential for primary prevention to evaluate the extent to which contributing risk factors are detected in the population in general, especially so among smokers who are already at an increased risk for CVD. Evidence suggests that over a third of people with diabetes (Mainous, III,

<sup>54</sup> QOF is part of the general practitioners contract and offers financial rewards to practices for adherence to quality of care indicators

Diaz, Saxena, Baker *et al.*, 2006) and more than a half of people with hypertension (Primatesta, Brookes, & Poulter, 2001) in England are either undiagnosed or unaware of their condition and although more recent data suggest this may have improved (Craig & Mindell, 2008), detection is still largely inadequate. Reports confirm that the information on heart disease in the UK is generally of mixed quality and that public health information on CVD needs to get better, e.g. by providing up-to-date population based estimates of risk factors, patient numbers etc (see Unal, Critchley, & Capewell, 2003). Many people likely to develop CVD are missed, and new methods to identify those with an increased risk profile such as cholesterol screening have therefore been proposed (e.g. Wilson, Johnston, Robson, Poulter *et al.*, 2003).

The issue of the detection of CVD and CVD risk factors is particularly pertinent for smokers as there is evidence that the diagnosis of CVD (e.g. Ockene, Hosmer, Rippe, Williams *et al.*, 1985) and related risk factors (e.g. Bovet, Perret *et al.*, 2002) as well as hospitalization owing to CVD (e.g. Di Tullio M., Granata, Taioli, Broccolino *et al.*, 1991; Rigotti, Singer, Mulley, Jr., & Thibault, 1991) all increase smoking cessation. Indeed, cardiac patients may be particularly receptive to smoking cessation interventions (France, Glasgow, & Marcus, 2001). This encouraging fact, however, is contrasted by the finding that smokers appear less likely to be treated for detected heart disease (Reid, Cook, & Whincup, 2002). It appears then that there is a need for better information on the smoking prevalence among people with CVD in order to tackle this issue.

Established biological markers such as triglycerides, HDL and LDL cholesterol (e.g. Castelli, Garrison, Wilson, Abbott *et al.*, 1986), fasting blood glucose (e.g. Kannel & McGee, 1979) and blood pressure (e.g. Kannel, 1975) have all been unequivocally

linked to an increased risk of CVD. More recently fibrinogen, and albumin and, less so, C-reactive protein (e.g. see Ernst & Resch, 1993; Danesh, Collins, Appleby, & Peto, 1998; Fibrinogen Studies Collaboration, 2005) have also been implied in the development of CVD. Consequently, these biomarkers are used both in the estimation of CVD risk (e.g. Wilson, D'Agostino, Levy, Belanger *et al.*, 1998) and for definitions of conditions such as the metabolic syndrome, which denotes the clustering of particular risk factors associated with CVD (Grundy, 1999; Sandhofer, Iglseder, Paulweber, Ebenbichler *et al.*, 2007). Biological markers of abnormal biophysiological functioning are therefore fundamental for the identification of people who either already have CVD or have an increased likelihood of developing CVD and by providing an objective measure of smoking status as well as disease occurrence, biological markers allow for an estimation of smoking prevalence in this vulnerable group of people.

### **IX.i.ii Aims**

This chapter uses data from the Health Survey for England to examine these issues in a nationally representative sample. Specifically, the aims were:

- 1) To describe smoking prevalence as well as smoking characteristics in people with CVD/CVD risk factors compared with smoking prevalence in people matched for age, gender and occupation<sup>55</sup> without CVD/CVD risk factors
- 2) To compare the level of diagnosis of CVD/CVD-related diseases in smokers and non-smokers.
- 3) To assess the association between receiving a diagnosis with a CVD/CVD-related disease and motivation to stop smoking as well as smoking cessation.

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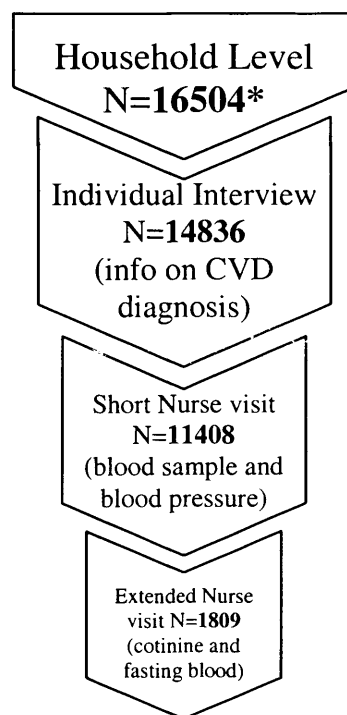
<sup>55</sup> As a proxy for socioeconomic status/deprivation

## IX.ii Methodology

### IX.ii.i Procedure and participants

Data are taken from the Health Survey for England (see VIII.ii.i for a description of HSE methodology), which in 2003 focused on risk factors for cardiovascular disease. Figure IX.I provides a breakdown of the number of adult participants (16 yrs of age and above)<sup>56</sup> at the various stages of the HSE.

**Figure IX.I: Flow-Chart Participants (16 yrs+)**



\*Estimate based on assumption of at least one adult in each eligible, non-responding household

Of eligible households, 73% (n=8867 households) took part in the 2003 survey, which had an effective sample size of 14836 participants (those who were interviewed) representing around 90% of the participating household sample. Data were collected at two visits; an interviewer administered a questionnaire and assessed anthropometric measures followed by a nurse visit a couple of days later. Three quarters of those undergoing an individual interview (and 70% of those living in participating

<sup>56</sup> This study excluded participants below 16 years of age as smoking-related (as opposed to congenital) cardiovascular disease, which is the focus of this Chapter, is virtually non-existent in children

households) had this short nurse visit, at which the use of prescribed medicines was recorded; it also comprised the collection of blood and the taking of blood pressure readings. At the interview stage, a small proportion of the effective sample (one sixth) had been randomised to receive an extended rather than a short nurse visit. Of those with an extended nurse visit, 44% agreed to have additional fasting blood and 65% salivary cotinine samples collected. A more detailed description of the 2003 HSE methodology can be found elsewhere (Blake, Deverill, Prescott, Primatesta *et al.*, 2004).

### **IX.ii.ii Measures**

#### **IX.ii.ii.i Demographic and anthropometric characteristics**

During the interview data on a range of demographic characteristics were collected including age, sex, ethnicity and occupational status (by head of household). The level of deprivation was assessed using the Index of Multiple Deprivation (IMD), a reliable measure of relative poverty based on post codes (Jordan, Roderick *et al.*, 2004). In addition, following a standard protocol (see Blake, Deverill *et al.*, 2004) anthropometric measures were taken at the nurse visit; waist circumference was measured and height as well as weight assessed to determine both central obesity and the body mass index (BMI; kg/m<sup>2</sup>).

#### **IX.ii.ii.ii Blood pressure and blood analytes**

Non-fasting blood samples were analysed for total cholesterol (TC), HDL cholesterol (HDL-C), C-reactive protein, glycated haemoglobin (Hb1AC) and fibrinogen. Fasting blood samples were assayed for triglycerides, glucose and LDL cholesterol<sup>57</sup>. Blood pressure was measured with the Omron HEM-907 at least 30 minutes after participants had last eaten, smoked, drunk alcohol or taken vigorous exercise. Three measurements

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<sup>57</sup> LDL cholesterol was determined by Friedewald formula; LDL cholesterol= total cholesterol – (HDL cholesterol+ (triglycerides/2.2))

were taken on the right arm after 5 minutes of rest and the mean of the last two readings were used in the analysis (for more details see Blake, Deverill *et al.*, 2004).

### **IX.ii.ii.iii Saliva cotinine**

Saliva samples were collected using a dental roll, which participants were asked to keep in the mouth until saturated. Samples were assayed for cotinine with a well established rapid gas liquid chromatography technique (Feyerabend & Russell, 1990). Cotinine is a major metabolite of nicotine that provides an extremely sensitive and specific quantitative measurement of smoking; in the absence of the use of nicotine replacement products saliva cotinine concentrations above 15 ng/ml usually indicate personal tobacco use (Jarvis, Tunstall-Pedoe *et al.*, 1987).

### **IX.ii.ii.iv Smoking characteristics**

Smoking status was assessed by self-report; participants were asked to indicate whether they had ever smoked. If participants replied yes, they were further asked whether they smoked currently and, if so, what type of tobacco (cigarettes, pipe, cigar). Based on the most recent response<sup>58</sup> smoking status was computed dividing participants into never smokers, ex-smokers, and current smokers (all types of tobacco) as well as current cigarette smokers. For those participants with valid cotinine<sup>59</sup>, results were used to adjust self-report and to estimate misreporting in this sample; cotinine concentrations above 15 ng/ml were taken to imply current smoking.

For current smokers, nicotine dependence was estimated with the Heaviness of Smoking Index (see VIII.ii.ii for details) and motivation to stop smoking with a single questionnaire item that asked smokers whether they would like to give up smoking

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<sup>58</sup> Depending on stage of HSE – if possible data from the nurse visit were used, if these were missing, data were imputed from the interview stage

<sup>59</sup> That is, sufficient saliva was collected to assess cotinine concentrations

altogether (yes/no). Smokers were also asked whether they had ever been advised to stop smoking by a health professional and if so, how long ago.

### **IX.ii.ii.v Cardiovascular disease and risk factors**

#### *Self-report*

During the interview, ischemic heart disease (IHD) was estimated using the Rose Angina Questionnaire, a validated tool to establish the presence of symptoms of angina (Pearson, Mensah, Alexander, Anderson *et al.*, 2003). Among others, participants were asked if they had ever experienced pain across the front of the chest lasting longer than half an hour. If participants replied 'Yes', they were further asked if they had seen a doctor because of the pain and, if so, what the doctor said it was. If participants reported the doctor said they had either angina or a heart attack, they were considered to be diagnosed with IHD. Moreover, participants were also asked if they have ever had a heart murmur<sup>60</sup>, stroke, abnormal heart rhythm or other heart trouble. If participants said 'Yes' to any of these questions, they were also asked if they had been told by a doctor what their condition was. Participants were considered to have been diagnosed with CVD<sup>61</sup> if they reported a doctor diagnosis with IHD, heart murmur, stroke, abnormal heart rhythm or other heart condition<sup>62</sup>.

The presence of doctor-diagnosed diabetes and hypertension was also assessed during the interview. In addition to being asked about their current use of medication (to control blood pressure, lipids or insulin levels), participants were also asked whether they ever had diabetes, and if so, if they had been told that they had diabetes by their doctor. If participants said 'Yes' to the latter two questions and/or reported taking insulin, they were considered to be diagnosed with diabetes mellitus<sup>63</sup>. Participants were

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<sup>60</sup> Participants pregnant at the time of diagnosis were excluded

<sup>61</sup> As hypertension was considered separately, it was not included in the definition of CVD here

<sup>62</sup> Data do not allow to determine what these heart conditions are but exclude congenital CVD

<sup>63</sup> Participants diagnosed with diabetes before 35 years of age were considered to have Type I diabetes

also asked if they have or have ever had high blood pressure, and if so, whether a doctor had told them they had hypertension<sup>64</sup>. If participants said 'Yes' to the latter two questions and/or if they reported taking medication to control blood pressure<sup>64</sup>, they were considered to have been diagnosed with hypertension.

Alcohol consumption in the last week was assessed by self report and excessive alcohol consumption ('binge drinking') defined as drinking twice the recommended daily amount of alcohol (8 units for men and 6 units for women) on at least one occasion in the past week following the Office for National Statistics definition (see Wilson, D'Agostino *et al.*, 1998). Physical activity was determined with a short questionnaire based on the Allied Dunbar National Fitness Survey (e.g. Rickards, Fox, Roberts, Fletcher *et al.*, 2004). Current guidelines recommend 30 min or more of moderate activity (defined as activity with energy cost  $\geq 5$  kcal/min) at least five times per week and participants were defined as inactive, or insufficiently active, if they did not reach this recommended level of exercise (Health Education Authority and Sports Council, 1992). Fruit and vegetable consumption was determined by questionnaire items that assessed intake over the preceding 24h in terms of everyday measures of consumption that were converted to standardized portion measures (80 g serving). In line with current recommendations, insufficient consumption was defined as having less than five portions of fruit or vegetables per day (Department of Health, 2000).

### *Objective assessment*

Data from biological markers were used to objectively define CVD risk factors. Using suggested cut-off values for increased CVD risk (e.g. see Bersot, Pepin, & Mahley, 2003; Banks, Marmot, Oldfield, & Smith, 2006), elevated TC to HDL-C ratio ( $\geq 5.5$ ) as

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<sup>64</sup> Participants were asked if they currently took medicines for high blood pressure, i.e. hypertension



well as raised C-reactive protein ( $\geq 3.0$  mg/L)<sup>65</sup> and fibrinogen levels ( $> 4.0$  g/L) were determined. Obesity was defined as having a BMI  $\geq 30$  kg/m<sup>2</sup>.

In addition, biomarkers were used to objectively verify a number of conditions that are associated with cardiovascular disease in general, and IHD in particular, namely hypertension, diabetes and the metabolic syndrome. Hypertension was defined as receiving blood pressure treatment or as having a systolic blood pressure of  $\geq 140$  mm Hg and/or a diastolic blood pressure of  $\geq 90$  mm Hg (e.g. see Williams, Poulter, Brown, Davis *et al.*, 2004). Diabetes<sup>66</sup> was defined as receiving treatment for diabetes, as having a fasting plasma glucose level of  $\geq 7.0$  mmol/L or as having glycated haemoglobin (Hb1AC) of above 6.1% (see Rohlfing, Little, Wiedmeyer, England *et al.*, 2000).

The presence of metabolic syndrome was defined using the International Diabetes Federation guidelines, which requires the presence of central obesity (based on waist circumference) together with any two of the following: raised triglycerides ( $>1.7$  mmol/L) or treatment for this lipid abnormality; reduced HDL cholesterol ( $< 1.03$  (men) or  $< 1.29$  (women) mmol/L) or treatment for this lipid abnormality; raised blood pressure (systolic blood pressure  $\geq 130$  mm Hg and/or a diastolic blood pressure of  $\geq 85$  mm Hg) or treatment for high blood pressure; and raised fasting plasma glucose ( $\geq 5.6$  mmol/L) or previously diagnosed diabetes (e.g. see Rohlfing, Little *et al.*, 2000). This method of determining the metabolic syndrome has been validated in a number of studies (Alberti, Zimmet, & Shaw, 2005).

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<sup>65</sup> Values above 10 mg/L were excluded as they are likely to indicate acute inflammation

<sup>66</sup> This excludes Type 1 Diabetes

Framingham-based risk equations<sup>67</sup> (e.g. Guerrero-Romero & Rodriguez-Moran, 2005; Wang, Ruotsalainen, Moilanen, Lepisto *et al.*, 2007) that employ age, sex, total and HDL cholesterol, blood pressure, smoking status and diabetes were used to estimate the 10 year risk of developing IHD.

### **IX.ii.iii Contributors**

The Health Survey for England is commissioned by the Department of Health and the Information Centre and carried out by the Joint Survey Unit of the National Centre for Social Research and the Department of Epidemiology and Public Health, University College London. The data were made available through the UK Data Archive. These bodies bear no responsibility for the analyses and interpretation of this Chapter. I conceived, devised and carried out this analysis. Jenny Mindell, Robert West and myself contributed to the interpretation of the data and I wrote up this Chapter.

### **IX.ii.iv Analysis**

Data were analysed using SPSS 14.0 and STATA 9.0. Parametric assumptions for continuous variables were examined by looking at histograms as well as the skewness and kurtosis of data<sup>68</sup> to assess normality of distribution and Levene's test to assess homogeneity of variance. As no variables failed assumptions, parametric tests alone were carried out. For continuous outcomes, group differences were tested with t-tests or, when controlling for confounders, ANCOVA. Group differences in dichotomous outcomes were tested with  $\chi^2$  analyses. Adjustments in proportions were calculated by the direct standardisation method using the total study population as the standard and group differences compared by Mantel-Haenszel test. Where appropriate, logistic regression analyses were conducted to evaluate associations between variables and to estimate odds ratios. In 2003, HSE data were weighted for the first time. However, in

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<sup>67</sup> These have been verified in Northern European populations

<sup>68</sup> Values between -1 and 1 were considered normal

order to ensure comparability with previous HSE analyses, only unweighted data are presented. Since this study used stratified, clustered sampling and to account for multiple comparisons, significance values were adjusted using the false discovery rate control (Benjamini & Hochberg, 1995).

### **IX.iii Results**

#### **IX.iii.i Description of demographic characteristics of the population according to CVD diagnosis**

In the population 16 years of age and above, 14.3% (N=2123; 95%CI 13.8-14.9) reported a CVD-related diagnosis and 5.8% (N=861; 95%CI 5.4-6.2) a diagnosis with IHD alone. There were 18 cases missing from this analysis who did not differ on any of the assessed socio-demographic variables. As shown in Table IX.II, those with diagnosed CVD were more likely to be older, male, in manual occupation and deprived than those without diagnosed CVD.

More than one in eight participants (13.1%, 95%CI 12.2-14.0) were at increased risk of CVD based on Framingham equations. However, neither those with a high ( $\geq 15\%$ ) 10 year IHD risk nor those with a very high ( $\geq 30\%$ ) 10 year IHD risk were any more or less likely to report being diagnosed with a CVD when controlling for age (OR 1.07, 95%CI 0.86-1.34 and OR 0.71, 95%CI 0.45-1.13, respectively; see Table IX.II). Of the 134 people with a 30% risk of IHD, only 24 unadjusted cases – that is less than a fifth (17.9 %, 95%CI 11.4-24.4 ) - reported any CVD diagnosis.

**Table IX.II: Sample characteristics by CVD diagnosis<sup>¶</sup> (16 years+)**

	Total Sample	No CVD diagnosis <sup>+</sup>	CVD diagnosis <sup>+</sup>
<b>Demographics</b>	<i>N=14836</i>	<i>N=12695</i>	<i>N=2123</i>
Mean (SD) age	48.2 (18.5)	46.0 (17.7)	61.4 (17.6)***
% (N) male	44.5 (6602)	44.1 (5598)	46.9 (996)*
% (N) manual occupation	39.6 (5872)	41.1 (4958)	44.3 (905)*
% (N) Lowest quintile IMD <sup>†</sup>	17.3 (2564)	16.8 (2127)	20.5 (436)***
<b>Smoking characteristics</b>			
% (N) Cigarette smoking prevalence	<i>N=14770</i>	<i>N=12651</i>	<i>N=2119</i>
Age 16-24	32.4 (520)	32.4 (496)	32.0 (24)
Age 25-34	33.8 (779)	33.3 (730)	41.2 (49)
Age 35-44	29.2 (840)	29.4 (782)	27.1 (57)
Age 45-54	25.3 (601)	24.9 (528)	28.3 (71)
Age 55-64	21.6 (520)	22.1 (438)	19.2 (81)
Age 65-74	14.1 (248)	14.3 (181)	13.9 (67)
Age 75+	8.8 (128)	9.5 (85)	7.7 (43)
All ages <sup>§</sup>		<i>N=12021</i>	<i>N=2037</i>
Current cigarette smoker	24.6 (3636)	24.9 (2991)	25.5 (521)
Current smoker	26.1 (3864)	26.5 (3190)	26.9 (551)
Ever Smoker	64.5 (9523)	65.0 (7804)	69.4 (1417)**
Mean (SD) cigarettes/day <sup>‡§</sup>	14.7 (8.3)	14.0 (9.9)	13.6 (8.1)
Mean (SD) saliva cotinine (ng/ml) <sup>§,¶</sup>	287 (194)	254 (237)	356 (187)***
Mean (SD) dependence rating <sup>‡,¶</sup>	3.6 (1.0)	3.6 (1.2)	3.5 (1.0)
% (N) Misreport of smoking status <sup>#</sup>	2.6 (42)	3.0 (41)	0.4 (1)*
% (N) Ever advised to quit by HP <sup>‡,¶</sup>	32.9 (1194)	28.9 (899)	61.3 (245)***
% (N) Advised to quit <1 year <sup>‡,¶</sup>	15.3 (556)	13.4 (416)	29.5 (118)***
% (N) Motivated to quit <sup>‡,¶</sup>	69.4 (2302)	68.1 (2007)	78.4 (284)***
<b>10 year IHD risk<sup>†</sup></b>	<i>N=5329</i>	<i>N=4652</i>	<i>N=670</i>
% (N) ≥ 15%	13.1 (699)	13.0 (603)	14.0 (94)
% (N) ≥ 30%	2.5 (134)	2.7 (125)	1.9 (13)

<sup>¶</sup> 18 cases missing; <sup>+</sup> Adjusted N are reported where indicated; <sup>‡</sup> Adjusted for age; <sup>§</sup> Adjusted for age, sex and occupation; <sup>§</sup> Cigarette smokers only; <sup>¶</sup> Excluding non-smokers and missing; <sup>†</sup> Adjusted for age and occupation; <sup>#</sup> Base N=1616; \* p<0.025, \*\*p<0.01; \*\*\*p<0.001

### **IX.iii.ii Smoking prevalence and smoking characteristics among those with and without CVD or CVD risk factors**

In terms of unadjusted values, those reporting a CVD diagnosis were less likely to be current cigarette smokers (18.5% vs. 25.6%,  $\chi^2(2)=49.5$ ,  $p<0.001$ ). However, when adjusting for age, sex and occupation, this difference in cigarette smoking prevalence was reduced to non-significance (OR 0.97, 95%CI 0.85-1.10) and the same applied to the consumption of any form of tobacco (OR 0.96, 95%CI 0.85-1.09, see Table IX.II). Irrespective of adjustment, people reporting a CVD diagnosis were more likely to have ever smoked and to have quit smoking (OR 1.21, 95%CI 1.08-1.35 and OR 1.15,

95%CI 1.01-1.32, respectively)<sup>69</sup>. In fact, there was an age by CVD diagnosis interaction for smoking prevalence, such that smoking prevalence declined more steeply across age groups among people reporting a CVD diagnosis (OR 0.94; 95%CI 0.92-0.97). For patients with reported IHD there were no significant differences in cigarette or any tobacco smoking prevalence and although those with reported IHD were more likely to have ever smoked (OR 1.37, 95%CI 1.15-1.63)<sup>69</sup>, they were not more likely to have quit smoking when controlling for confounders (OR 1.21, 95%CI 0.98-1.48)<sup>69</sup>.

While smokers with reported CVD were no more dependent than smokers without CVD according to self-reported cigarette consumption or HSI, they displayed higher salivary cotinine concentrations even after adjusting for confounders ( $F(1,437)=13.0$ ,  $p<0.001$ ). Interestingly, smokers with a diagnosed CVD were less likely to misreport themselves as non-current smokers compared with smokers without reported cardiovascular diseases (OR 0.13, 95%CI 0.18-0.99)<sup>69</sup>. Lastly, smokers with a diagnosed CVD were not only significantly more likely to have been advised to stop smoking by a health professional (OR 4.55, 95%CI 3.62-5.71)<sup>69</sup> and to have been advised more recently (OR 2.87, 95%CI 2.23 -3.69)<sup>69</sup>, but they were also more likely to be interested in quitting (OR 1.78, 95%CI 1.36 -2.33)<sup>69</sup>.

As can be seen in Table IX.III, diagnosed or undiagnosed hypertension was by far the most prevalent of the three CVD-related diseases that were assessed (33.4%; 95%CI 32.7 -34.2), and only people with high blood pressure were less likely to be smokers (OR 0.82, 95%CI 0.75-0.90) or cigarette smokers (OR 0.83, 95%CI 0.75-0.91). By contrast, smoking rates did not differ significantly between those with and without either diabetes or the metabolic syndrome (all  $p>0.10$ ).

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<sup>69</sup> Controlling for relevant confounders (see Table IX.II)

**Table IX.III: Smoking prevalence by disease-related CVD risk factors<sup>#</sup>**

Disease distribution, % (N) <sup>+</sup>		Prevalence; % <sup>§</sup>		
		Cigarette smoking <sup>‡</sup>	Any smoking <sup>‡</sup>	Ever smoking <sup>‡</sup>
High blood pressure (N=14836)	Y: 33.4 (4960)	24.2	25.8	65.2
	N: 66.6 (9876)	26.1***	27.7***	65.9
Diabetes Mellitus (N=14836)	Y: 5.5 (822)	27.1	28.6	65.5
	N: 94.5 (14014)	24.8	26.4	65.2
Metabolic Syndrome (N=5853)	Y: 20.1 (1178)	19.5	20.8	65.5
	N: 79.9 (4675)	22.4	23.7	67.8

<sup>#</sup>Disease by self-report/treatment or objective marker; <sup>+</sup>Y-Yes, N-No; <sup>§</sup>All values shown adjusted for age, sex and occupation; <sup>‡</sup> Comparisons are within each group, between those with (Y) and without (N) each risk factor; \*\*\*p<0.001

In terms of smoking-related characteristics, those with either hypertension, diabetes or the metabolic syndrome were more likely to have received quit advice (OR 1.61, 95%CI 1.37-1.89; OR 2.08, 95%CI 1.71-2.54 and OR 1.87, 95%CI 1.56-2.24, respectively)<sup>69</sup>. However, only people with diabetes were more likely to have been recently (less than year ago) advised to stop compared with smokers without self-reported or objectively determined diabetes (OR 1.68, 95%CI 1.10-2.58)<sup>69</sup>. Although participants with hypertension were less likely to smoke than those with diabetes or the metabolic syndrome, only smokers with the latter two diseases were inclined towards wanting to stop smoking compared with smokers without diabetes or the metabolic syndrome (OR 1.76, 95%CI 1.17-2.65 and OR 1.65, 95%CI 1.12-2.45, respectively)<sup>69</sup>. Cigarette smokers with diabetes were also more dependent as indicated by higher number of cigarettes smoked per day ( $F(1,3242)=6.5$ ,  $p=0.011$ )<sup>69</sup>.

Of the three assessed CVD risk biomarkers, elevated C-protein was most common (26.5%, 95%CI 25.5-27.5) and both raised TC:HDL-C and fibrinogen were detected at comparable rates (see Table IX.IV). People with signs of elevated risk biomarkers were significantly more likely to be current cigarette smokers, smokers of any tobacco or to have ever smoked.

**Table IX.IV: Smoking prevalence by biomarker-related CVD risk factors<sup>#</sup>**

Risk factor distribution, % (N) <sup>+</sup>		Prevalence; % <sup>§</sup>		
		Cigarette smoking <sup>‡</sup>	Any smoking <sup>‡</sup>	Ever smoking <sup>‡</sup>
Elevated Total-C: HDL-C ratio (N= 8274)	Y: 10.2 (847)	32.5	34.5	68.7
	N: 89.8 (7427)	22.1***	23.7***	65.0**
Elevated C-reactive protein (N=7701)	Y: 26.5 (2043)	27.3	29.0	67.3
	N: 73.5 (5658)	21.3***	23.1***	64.4**
Elevated Fibrinogen (N=6973)	Y: 8.1 (566)	37.7	39.1	71.7
	N: 91.9 (6407)	23.2***	25.0***	64.6**

<sup>#</sup>For definition of risk factor cut-offs see IX.ii.ii; <sup>+</sup>Y-Yes, N-No; <sup>§</sup>All values shown adjusted for age, sex and occupation; <sup>‡</sup> Comparisons are within each group, between those with (Y) and without (N) each risk factor; \*\*p<0.01; \*\*\*p<0.001

Smokers with elevated biomarkers also shared a number of characteristics. Except for those with high fibrinogen levels, smokers with elevated risk biomarkers appeared more dependent than those without them even after controlling for confounders. For instance, smokers with an elevated TC:HDL-C ratio consumed more cigarettes ( $F(1, 1727)=8.9$ ,  $p=0.003$ ), had a greater HSI ( $F(1, 1665)=6.1$ ,  $p=0.014$ ) as well as higher cotinine levels ( $F(1, 328)=5.8$ ,  $p=0.016$ ) than those with a normal TC:HDL-C ratio. Higher levels of cigarette consumption, HSI and cotinine were also found in smokers with elevated C-reactive protein. While people with elevated CVD risk biomarkers were more likely to smoke and to be more dependent, only smokers with high fibrinogen or C-reactive protein levels were more likely to have been advised to stop smoking (OR 1.67, 95%CI 1.30-2.15 and OR 1.45, 95%CI 1.24-1.70, respectively). Moreover, smokers with any of these CVD risk biomarkers were not more inclined towards cessation or to have been advised to stop smoking within the last year (all  $p>0.10$ ).

As shown in Table IX.V, consuming fewer than five portions of fruit or vegetable per day was the most common lifestyle-related CVD risk factor (75.5%, 95%CI 74.8-76.2) closely followed by having a sedentary/inactive lifestyle; excessive alcohol and food consumption were less prevalent. With the exception of obese or inactive people, those

adapting a lifestyle conducive to CVD were also significantly more likely to currently smoke. In general, smokers with a lifestyle risk factor were more dependent controlling for age, sex and occupation. Smokers who drunk excessively or were obese consumed more cigarettes ( $F(1, 2281)=42.5$ ,  $p<0.001$  and  $F(1, 2932)=14.3$ ,  $p<0.001$ , respectively) and had a greater self-reported level of dependence ( $F(1, 2220)=39.8$ ,  $p<0.001$  and  $F(1, 2849)=10.8$ ,  $p<0.001$ , respectively). In addition, smokers with a low fruit or vegetable consumption also had higher cotinine concentrations ( $F(1, 437)=5.5$ ,  $p=0.019$ ). Only obese or inactive smokers, however, were more likely than those without this risk factor to have been advised to stop smoking (OR 1.19, 95%CI 1.05-1.35 and OR 1.44, 95%CI 1.24-1.69, respectively). However, smokers with any of the lifestyle CVD risk factors did not report having been advised to quit more recently or to want to stop smoking more than smokers without these risk factors.

**Table IX.V: Smoking prevalence by lifestyle-related CVD risk factors<sup>#</sup>**

Risk factor distribution, % (N) <sup>+</sup>		Prevalence; % <sup>\$</sup>		
		Cigarette smoking <sup>‡</sup>	Any smoking <sup>‡</sup>	Ever smoking <sup>‡</sup>
Inactive lifestyle (N=14791)	Y: 71.1 (10519)	25.8	27.2	65.1
	N: 28.9 (4272)	23.9	25.6	65.3
Obese (N=13056)	Y: 23.2 (3030)	21.1	22.9	66.4
	N: 76.8 (10026)	26.9***	28.5***	65.6
High alcohol consumption (N=9977)	Y: 22.8 (2271)	39.7	42.1	79.3
	N: 77.2 (7706)	22.4***	24.1***	66.8***
Low fruit/veg consumption (N=14836)	Y: 75.5 (11196)	27.9	29.6	66.7
	N: 24.5 (3640)	15.1***	16.5***	61.1***

<sup>#</sup>For definition of risk factor cut-offs see IX.ii.ii; <sup>+</sup>Y-Yes, N-No; <sup>\$</sup>All values shown adjusted for age, sex and occupation; <sup>‡</sup> Comparisons are within each group, between those with (Y) and without (N) each risk factor; \*\* $p<0.01$ ; \*\*\* $p<0.001$

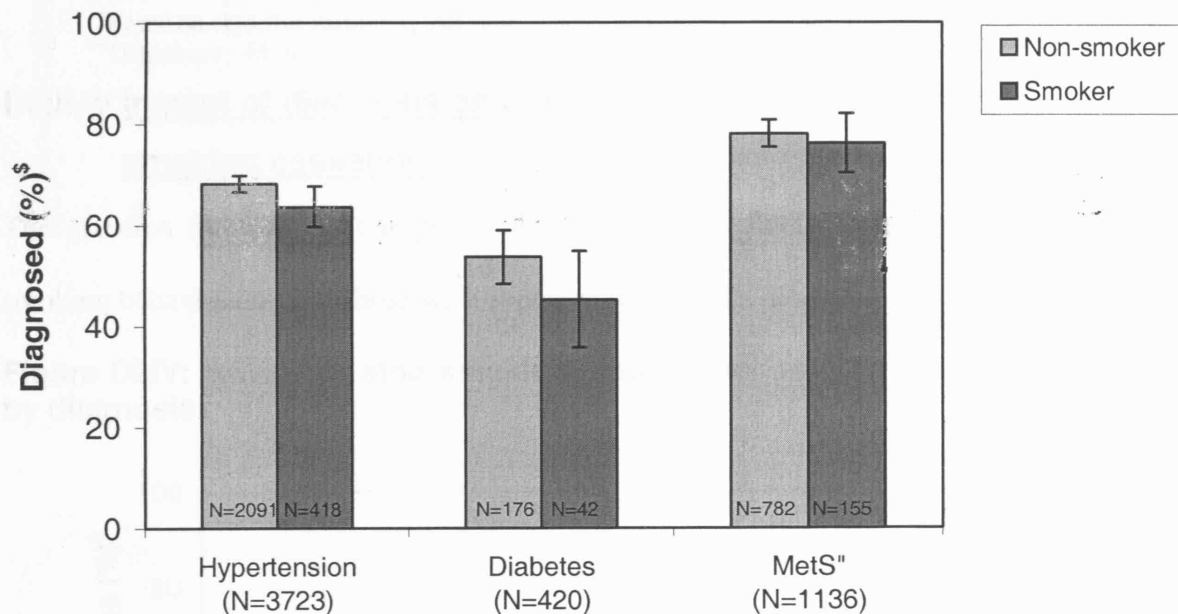
### **IX.iii.iii Diagnosis of CVD-related diseases among smokers and non-smokers**

In order to estimate whether smokers were more likely to be diagnosed with a CVD-related disease, the detection of hypertension, diabetes or any CVD was determined



among people with objective signs of hypertension, diabetes or the metabolic syndrome (MetS), respectively. As can be seen in Figure IX.II, current smokers were not more likely to have been diagnosed with any of these diseases. In fact, among people who show objective signs of hypertension, smokers were less likely to be diagnosed with hypertension than non-smokers even after controlling for socio-demographic variables and blood pressure (OR 0.69, 95%CI 0.56-0.85). The same was true when comparing current with ex-smokers (OR 0.63, 95%CI 0.50-0.78) or never smokers (OR 0.76, 95%CI 0.60-0.97).

**Figure IX.II: Diagnosis level among people with disease<sup>#</sup> by current smoking**

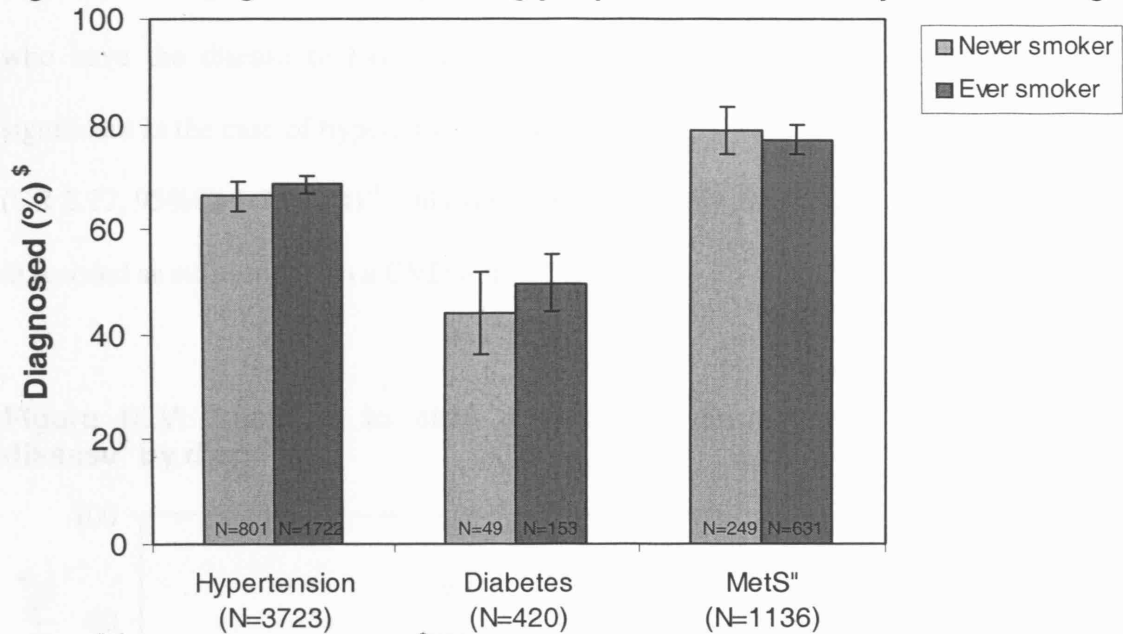


<sup>#</sup>Based on objective measures; <sup>\$</sup>All values shown adjusted for age, sex and occupation;

<sup>°</sup>Diagnosed with any CVD

While this difference in being diagnosed disappeared when comparing hypertensive ever-with never smokers (OR 1.09, 95%CI 0.92-1.29)<sup>70</sup>, as before ever smokers with objective signs of CVD-related diseases were not more likely than never smokers to be diagnosed with diabetes or the metabolic syndrome (see Figure IX.III).

<sup>70</sup> Adjusted for age, sex and occupation

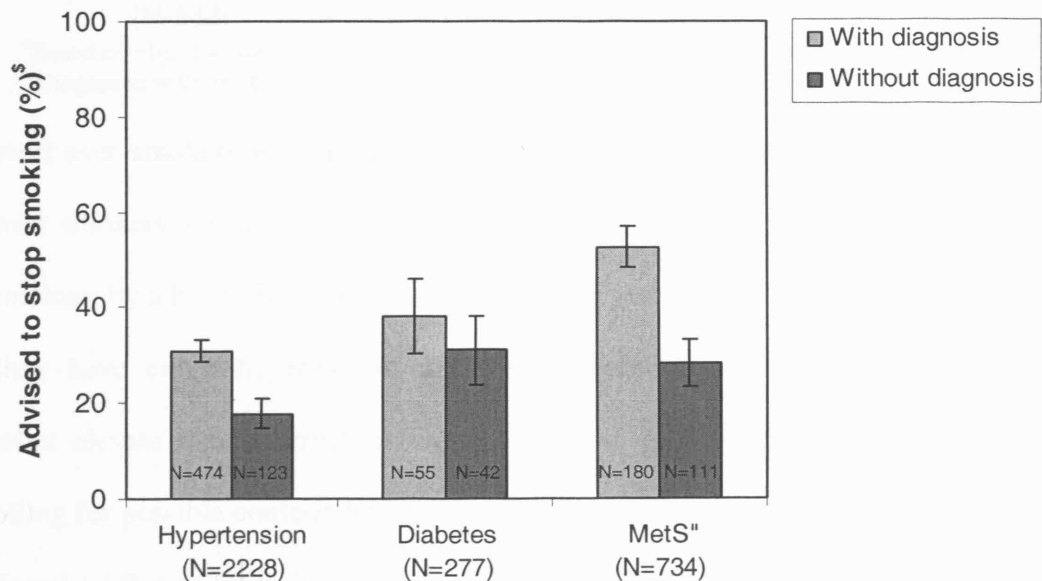
**Figure IX.III: Diagnosis level among people with disease<sup>#</sup> by ever smoking**

<sup>#</sup>Based on objective measures; <sup>\$</sup>All values shown adjusted for age, sex and occupation;

<sup>''</sup>Diagnosed with any CVD

#### **IX.iii.iv Impact of diagnosis on intention to stop smoking and smoking cessation**

The question remains what impact a diagnosis with a CVD-related disease has on smoking behaviour among those with objective signs of the disease.

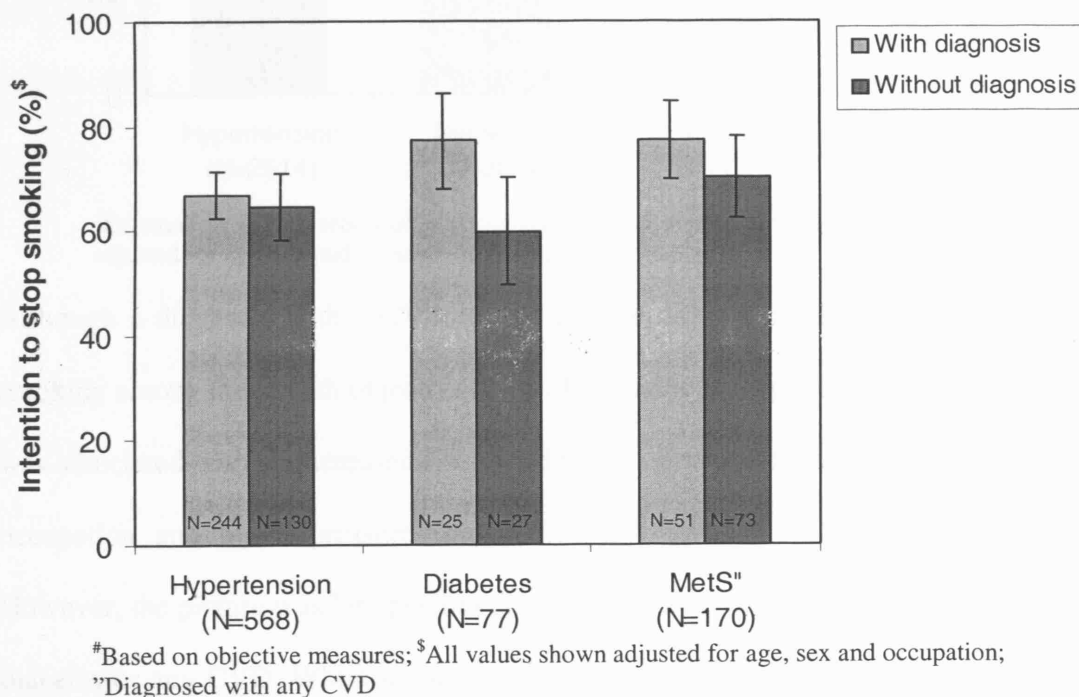
**Figure IX.IV: Advice to stop smoking among ever smokers with disease<sup>#</sup> by diagnosis**

<sup>#</sup>Based on objective measures; <sup>\$</sup>All values shown adjusted for age, sex and occupation;

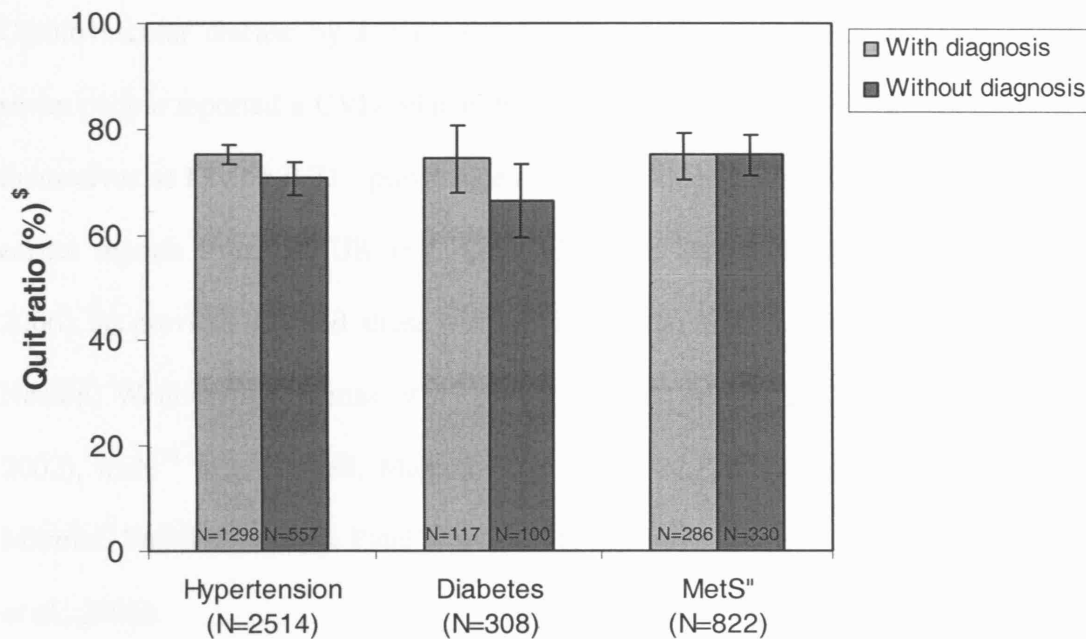
<sup>''</sup>Diagnosed with any CVD

As shown in Figure IX.IV, being diagnosed increased the likelihood for ever smokers who have the disease to have been advised to stop smoking. This difference was significant in the case of hypertensive ever smokers who were told about their condition (OR 2.17, 95%CI 1.73-2.74)<sup>70</sup> and ever smokers with the metabolic syndrome who were diagnosed as suffering from a CVD (OR 3.17, 95%CI 2.25-4.46)<sup>70</sup>.

**Figure IX.V: Intention to stop smoking among current smokers with disease<sup>#</sup> by diagnosis**



However, ever smokers with a diagnosed CVD-related disease were not more likely than ever smokers with an undiagnosed CVD-related disease to have been advised to stop smoking by a health professional within the last year (all  $p > 0.10$ ). Telling smokers that they have either hypertension, diabetes or some form of CVD may indeed somewhat elevate their motivation to stop smoking (see Figure IX.V). Yet, when controlling for possible confounders, this increase in smokers' intention to quit was not significantly different from the quit intentions of smokers who have a disease but have not been diagnosed (all  $p > 0.10$ ).

**Figure IX.VI: Quit ratio<sup>~</sup> among people with disease<sup>#</sup> by diagnosis**

<sup>~</sup>Ex-smokers as proportion of ever smokers; <sup>#</sup>Based on objective measures; <sup>\$</sup>All values shown adjusted for age, sex and occupation; <sup>~</sup>Diagnosed with any CVD

Although a diagnosis with a CVD-related disease did not increase motivation to stop smoking among those with objective signs of a disease, being identified as hypertensive was associated with an increased likelihood to stop smoking after adjusting for age, sex, occupation and blood pressure level (OR 1.57, 95%CI 1.25-1.97; Figure IX.VI). However, the picture was less positive for those smokers who received a diagnosis with diabetes or any CVD. While it was certainly the case that fewer people with diabetes, though not with the metabolic syndrome, smoked when they reported a correct diagnosis compared with people unaware of their condition, this difference was not significant in terms of its impact on the quit ratio.

#### **IX.iv Discussion**

This is one of only a handful of studies evaluating the smoking prevalence among people with either established CVD or extant CVD risk factors; it highlights the need for a continuing effort to address the issue of smoking in this vulnerable population.

**IX.iv.i Prevalence of CVD and CVD-related diseases and risk factors**

Cardiovascular disease by self-report was relatively common in this sample; one in seven people reported a CVD-related diagnosis and more than one in twenty identified themselves as having IHD - prevalence estimates which are broadly in agreement with earlier reports from the UK (e.g. Leyland, 2005; Strong, Maheswaran, & Radford, 2006). As previously found, those with cardiovascular diseases were older, (e.g. Kannel, Neaton, Wentworth, Thomas *et al.*, 1986; Peeters, Mamun, Willekens, & Bonneux, 2002), male<sup>71</sup> (e.g. Carroll, Majeed, Firth, & Gray, 2003) and more deprived (e.g. Marmot, Smith, Stansfeld, Patel *et al.*, 1991; Murphy, Simpson, MacIntyre, McAlister *et al.*, 2006).

The prevalence of CVD-related diseases was similar to that in previous reports. Hypertension was present in around a third of the sample, which is analogous to estimates from a range of other countries (e.g. Jo, Ahn, Lee, Shin *et al.*, 2001; Wolf-Maier, Cooper, Banegas, Giampaoli *et al.*, 2003). Whilst the prevalence of the metabolic syndrome varies widely owing to differences in the population sampled and the criteria used (Abate, 2000), the current estimate that one in five people displayed signs of the syndrome is in keeping with other reports, irrespective of the definition used in these studies (see Park, Zhu, Palaniappan, Heshka *et al.*, 2003; Ford, 2005; Perel, Langenberg, Ferrie, Moser *et al.*, 2006; Sandhofer, Iglseider *et al.*, 2007). Diabetes mellitus, which, similar to other reports (Mainous, III, Diaz *et al.*, 2006; Banks, Marmot *et al.*, 2006; Smith, Jr., 2007) had a population distribution of around five percent, was by far the least common of the assessed CVD-related diseases.

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<sup>71</sup> Some studies, however, report comparable overall CVD prevalence among men and women (see Callow, 2006) as especially in older age, the incidence of CVD among women starts to catch up with that among men

The prevalence of elevated CVD risk biomarkers was comparable to previous analyses (Ajani, Ford, & McGuire, 2006). In terms of lifestyle-related risk factors for CVD other than smoking, reduced fruit and vegetable consumption was particularly common, which has also been previously observed in this (Poortinga, 2007) and other populations (Serdula, Gillespie, Kettel-Khan, Farris *et al.*, 2004). In addition, prevalence estimates for obesity, excessive alcohol consumption and levels of inactivity all broadly corresponded to previous reports (e.g. Centers for Disease Control and Prevention, 1997; Hallal, Victora, Wells, & Lima, 2003; Sengupta & Hoyle, 2005; Raistrick, 2005; Rennie & Jebb, 2005).

### **IX.iv.ii Smoking and smoking characteristics among those with CVD and CVD-related diseases and risk factors**

The unadjusted cigarette smoking prevalence among people with self-reported CVD was comparable to previous estimates from European countries including the UK (EUROASPIRE II Study Group, 2001) but was lower than in some other countries (EUROASPIRE Study Group, 1997; Sonmez, Akcay, Akcakoyun, Demir *et al.*, 2002; Khot, Khot, Bajzer, Sapp *et al.*, 2003; Hammoudeh, Al-Tarawneh, Elharassis, Haddad *et al.*, 2006). Yet, the cigarette smoking prevalence was not significantly different for those either reporting or not reporting a diagnosis with a CVD after controlling for a number of confounders; nearly a quarter of people in the former group were current cigarette smokers. Including cigar and pipe smoking in the analysis, did not change these results<sup>72</sup>. In addition, self-reported IHD was not associated with lower tobacco or cigarette smoking prevalence, which is in keeping with studies showing that many smokers continue to smoke (e.g. Baile, Jr., Bigelow, Gottlieb, Stitzer *et al.*, 1982) or relapse soon after acute IHD events (e.g. van Berkel, van, V, & Boersma, 2000).

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<sup>72</sup> This is consistent with the lower risk of cardiovascular problems associated with both cigar and pipe smoking as opposed to cigarette smoking (Doll, Peto *et al.*, 1994; Wald & Watt, 1997; Baker, Ainsworth, Dye, Crammer *et al.*, 2000)

Generally, people with diagnosed CVD were more likely to have ever smoked than those without diagnosis but this prevalence estimate was somewhat higher than in a French study (Bongard, Cambou, Lezorovcz, Ferreres *et al.*, 2004). Consistent with an observed increase in smoking rates among younger CVD patients (EUROASPIRE I and II Group, 2001), in our study smoking prevalence among people reporting a CVD diagnosis was highest in younger age groups. The decrease in smoking prevalence as people with CVD become older shows that the overall smoking prevalence in this group represents the balance between an increased rate of ever-smoking (leading to the early development of CVD) and reduced rates of current smoking at a later stage, either because smokers with CVD are more likely to quit or, more probable, because they die younger compared with non-smoking CVD patients. Those with CVD were also more dependent according to objective markers, which suggests that these are hard-core smokers (Campbell, Prescott, & Tjeder-Burton, 1996; John, Meyer, Hanke, Volzke *et al.*, 2006) as they are unable to stop smoking despite the presence of a cardiovascular disease. This phenomenon has also been observed in other smoking-related illnesses such as lung cancer or chronic obstructive pulmonary disease (Kunze, Schoberberger, Fagerström, Aigner *et al.*, 1996; Jimenez-Ruiz, Masa, Miravittles, Gabriel *et al.*, 2001). In terms of CVD-related illnesses, smoking prevalence was not significantly reduced among people with diabetes, which is in agreement with previous reports showing that smoking rates are similar for diabetics and non-diabetics (e.g. Ford, Malarcher, Herman, & Aubert, 1994; Gulliford, Sedgwick, & Pearce, 2003; but see Zaninotto, Mindell, & Hirani, 2007). Smoking despite the presence of diabetes may be the result of greater nicotine dependence observed in this group of smokers. There were also no significant differences in terms of smoking among those with and without the metabolic syndrome. The literature is somewhat mixed on this issue as many studies find an association

between smoking and the metabolic syndrome (Park, Zhu *et al.*, 2003; Park, Oh, Cho, Choi *et al.*, 2004; Miyatake, Wada, Kawasaki, Nishii *et al.*, 2006) while others do not (e.g. Lidfeldt, Nyberg, Nerbrand, Samsioe *et al.*, 2003; Ford, 2005; Yoon, Lee, Park, Lee *et al.*, 2007). Of the CVD-related diseases considered, only hypertension was associated with a reduction in smoking prevalence. Yet, the few studies that have compared hypertensive with normotensive individuals have found both lower (Hunt, Hopton, Padfield, & Holton, 1990) and equal smoking rates (Nothwehr, Elmer, & Hannan, 1994; Lu, Tang, Wu, Yang *et al.*, 2000) for hypertensive patients.

Considering the relationship between biological markers of CVD risk and smoking, there was a consistent linkage between increased risk biomarker levels and smoking rates as well as nicotine dependence. This is a well-reported association, which has been found with respect to C-reactive protein (Mendall, Strachan, Butland, Ballam *et al.*, 2000), fibrinogen (Bazzano, He, Muntner, Vupputuri *et al.*, 2003) as well as blood lipids such as HDL cholesterol (e.g. Costanza, Cayanis, Ross, Flaherty *et al.*, 2005). This finding is most likely indicative of a causal relationship that exists between smoking and human systemic haemostatic and inflammatory responses, which may mediate the onset of cardiovascular diseases (e.g. see Wannamethee, Lowe, Shaper, Rumley *et al.*, 2005; Yanbaeva, Dentener, Creutzberg, Wesseling *et al.*, 2007). Thus people who smoke are more likely to display higher levels of such biomarkers and the more people smoke (i.e. the more dependent they are) the more pronounced this physiological response becomes and the more likely they are to develop CVD.

In agreement with findings from the current study, a substantial body of evidence suggests that with the exception of overweight and obesity (e.g. Albanes, Jones, Micozzi, & Mattson, 1987; Canoy, Wareham, Luben, Welch *et al.*, 2005) there is a



strong link between various unhealthy lifestyle choices and smoking (e.g. unhealthy diet: Oshaug, Bjornes, Bugge, & Trygg, 1996; Liu, Manson, Lee, Cole *et al.*, 2000; excessive alcohol consumption: Romberger & Grant, 2004; inactivity: Pitsavos, Panagiotakos, Lentzas, & Stefanadis, 2005). Smokers in this study who reported an unhealthy lifestyle were also more dependent on cigarettes. Altogether, this hints at a 'clustering' effect, i.e. the phenomenon that people tend to consistently engage in either a detrimental or positive health behaviour pattern (Laaksonen, Prattala, & Karisto, 2001; Tobias, Jackson, Yeh, & Huang, 2007; Poortinga, 2007). Clustering of risky health behaviours tends to occur in particular groups, such as younger or more deprived individuals (e.g. Schuit, van Loon, Tijhuis, & Ocke, 2002; Pronk, Anderson, Crain, Martinson *et al.*, 2004; Fine, Philogene, Gramling, Coups *et al.*, 2004) and has therefore been suggested as possibly contributing to the socioeconomic gradient in disease morbidity and mortality (see van Oort, van Lenthe, & Mackenbach, 2004).

### **IX.iv.iii Detection of CVD and CVD-related diseases, associated quit advice and impact on smoking cessation**

Somewhat surprising, people who displayed either a high or very high 10 year risk to develop IHD and thus, according to guidelines, are in need of urgent identification to be prioritised for appropriate and immediate treatment (Wood, Durrington, McInnes, Poulter *et al.*, 1998), were no more or less likely to have been diagnosed with any CVD. Indeed, only a fifth of people with a very high risk of IHD reported any CVD diagnosis. This underlines an existing concern for an improvement in the detection of individuals who are most likely to develop CVD (e.g. see Simon & Levenson, 2005). While the level of detection of diabetes was comparable to that in other analyses (e.g. Faeh, William, Tappy, Ravussin *et al.*, 2007), the proportion of people with the metabolic syndrome who reported a cardiovascular condition was much higher in this than in a Canadian sample (Anand, Yi, Gerstein, Lonn *et al.*, 2003).

The self-reported level of detection of hypertension was equivalent to UK-based estimates from other analyses (Wolf-Maier, Cooper, Kramer, Banegas *et al.*, 2004; Craig & Mindell, 2007) and compared favourably to hypertension awareness reported in different countries (e.g. Aubert, Bovet, Gervasoni, Rwebogora *et al.*, 1998; Macedo, Lima, Silva, Alcantara *et al.*, 2005). It is noteworthy that a number of other studies have found evidence of a reduced level of awareness or detection of hypertension in smokers compared with non-smokers (see Gulliford, 2001; Zachariah, Thankappan, Alex, Sarma *et al.*, 2003), which was also the case in this study. The results would suggest that current smokers are less likely to be identified as hypertensives than either ex- or never smokers though it is possible that this finding is an artefact of the study design. It may be that smokers are more likely to 'forget' or 'not remember' a diagnosis with hypertension. However, it is unclear why the same would not also apply to a diagnosis with CVD or diabetes as there was no evidence of a differential rate of diagnosis for these diseases among smokers and non-smokers. Alternatively, and perhaps more plausible, smokers who are diagnosed were - as was shown - more likely to stop smoking thus possibly resulting in a greater pool of undiagnosed hypertensive smokers.

Whatever the explanation, this finding is concerning for two reasons. First, evidence has started to accumulate challenging the idea that smoking has hypotensive action – rather, it appears, the opposite may be true (Pardell & Rodicio, 2005). Current smoking has been shown to increase blood pressure when this is measured not on one occasion, as is commonly the case, but over 24 hours (e.g. Verdecchia, Schillaci, Borgioni, Ciucci *et al.*, 1995). This is most likely due to the vasoconstrictor effects of nicotine (Benowitz, 1997) and implies that smoking may actually exacerbate undetected hypertension as shown by the raised risk to develop malignant hypertension among smokers with high

blood pressure (Isles, Brown, Cumming, Lever *et al.*, 1979). Second, although both smoking and hypertension independently increase CVD risk, concurrently they also synergistically interact resulting in a more than four-fold increase in the risk of developing IHD (Kannel, 1995). Thus smokers with hypertension who are not identified are not only more likely to increase the severity of hypertension but are also at a much greater risk to suffer from a serious CVD event.

As reported elsewhere (e.g. Maguire, Ryan, Kelly, O'Neill *et al.*, 2000; Ossip-Klein, McIntosh, Utman, Burton *et al.*, 2000; Lucan & Katz, 2006) most smokers with self-reported or objectively determined CVD and CVD-related diseases and risk factors were more likely to have been advised to stop smoking than smokers without these. The prevalence of quit advice was very similar to that in previous studies (e.g. Parnes, Main, Holcomb, & Pace, 2002) but does not appear to have increased over the last twenty years (see Fortmann, Sallis, Magnus, & Farquhar, 1985; Anda, Remington, Sienko, & Davis, 1987); only about half of smokers with diseases recalled being advised to stop. Indeed, some studies suggest a decline in quit advice (Wallace, Sairafi, & Weeks, 2006), and in the current study smokers with CVD-related diseases and risk factors were generally not more likely to have been advised to stop smoking within the last year.

The disappointing rate of quit advice provided by health professionals is likely to be the result of a number of barriers including a lack of confidence in the ability to provide adequate advice and a lack of belief in the efficacy of providing quit advice (see Wells, Lewis, Leake, Schleiter *et al.*, 1986; Kottke, Willms, Solberg, & Brekke, 1994; Cabana, Rand, Powe, Wu *et al.*, 1999). Moreover, it seems that the level of advice provided is influenced by having an appropriate diagnosis; having a disease but not being diagnosed

significantly decreased the likelihood of having ever received quit advice thus smokers with objective signs of disease who are missed are even less likely to be advised to quit.

This is important because a diagnosis with chronic disease has been found to double the odds of smoking cessation (Novotny, Fiore, Hatziaandreu, Giovino *et al.*, 1990; see McWhorter, Boyd, & Mattson, 1990; Salive, Cornoni-Huntley, LaCroix, Ostfeld *et al.*, 1992). However, although being diagnosed with a CVD-related disease was associated with receiving quit advice in this sample, it was not associated with an increase in motivation to stop smoking. Yet, as has been previously suggested (e.g. Kastarinen, Tuomilehto, Vartiainen, Jousilahti *et al.*, 2002; John, Meyer *et al.*, 2006) hypertensive individuals with a disease diagnosis were more likely to have stopped smoking than hypertensives who went undetected. In contrast, there was no diagnosis-dependent difference in quit rates among those with the metabolic syndrome or diabetes, which may - at least in case of diabetics – be related to greater nicotine dependence attenuating the impact of a diagnosis and associated quit advice on smoking cessation.

### **IX.iv.iv Limitations**

This study has a number of limitations, which need to be considered when evaluating the results. First, as data came from a cross-sectional survey, they do not allow for conclusions about causal relations to be drawn. However, the Health Survey for England is a large, well-designed and methodologically rigorous study providing nationally representative data, and in the absence of adequate longitudinal surveys, cross-sectional studies such as this may at least help elucidate some of these associations.

Second, most of the data used in the analysis, such as doctor diagnosis, smoking status and quit advice, were based on self-report. Yet, evidence suggests that self-reported

CVD is valid measure of an actual diagnosis (Lampe, Walker, Lennon, Whincup *et al.*, 1999), that the impact of misreporting on smoking prevalence is relatively small (e.g. Vartiainen, Seppala, Lillsunde, & Puska, 2002; but see West, Zatonski *et al.*, 2007) and that, if anything, self-report overestimates the provision of quit advice (Wilson & McDonald, 1994; Ward & Sanson-Fisher, 1996).

Third, disease estimates, especially hypertension, may have been overestimated since - contrary to current recommendations (Ramsay, Williams, Johnston, MacGregor *et al.*, 1999) - blood pressure was not measured on successive occasions. However, methodological precautions were taken to reduce this risk (e.g. a nurse, not a physician measured blood pressure; people who had engaged in activities that raise blood pressure within half an hour were excluded), and prevalence estimates were comparable to the literature. Similarly, while there is some controversy regarding the measurement of the metabolic syndrome in general (Federspil, Nisoli, & Vettor, 2006), and following IDF guidelines in particular (Chen & Pan, 2007), as well as some doubt about the use of glycated proteins (i.e. GHb) to determine diabetes (Sacks, Bruns, Goldstein, Maclaren *et al.*, 2002), the fact that prevalence estimates were comparable to other studies would indicate that results were not unduly influenced by these factors.

Fourth, psychiatric comorbidity was not assessed and this may have influenced results as those with psychiatric illnesses are both more likely to be smokers (West & Jarvis, 2005) and to have a physical illness (Evans, Charney, Lewis, Golden *et al.*, 2005). However, not only is the effect of psychiatric comorbidity on the whole sample likely to be limited, but the study also took into consideration other potential confounders associated with both smoking and psychiatric comorbidity such as occupation/deprivation and nicotine dependence.

Fifth, it is well known that smokers are more likely to display optimistic bias and have self-exempting beliefs regarding the risks of smoking in order to reduce cognitive dissonance (e.g. Chapman, Wong, & Smith, 1993). It may therefore be possible that people with a disease who continue to smoke may also be less likely to report either being diagnosed with a disease or being advised to stop smoking so as to maintain cognitive consonance. However, this is unlikely to have affected results as not only is there evidence that smokers with a disease are actually more likely to report receiving quit advice (e.g. Nicholson, Hennrikus, Lando, McCarty *et al.*, 2000) but also no differences between smokers and non-smokers in terms of the accuracy of self-reported disease diagnosis have been found (e.g. Bergmann, Byers, Freedman, & Mokdad, 1998).

Lastly, since the publication of data (2003) a number of smoking-relevant policies and changes have been put into place. In addition to an expansion in the licensing remit of NRT to include prescription of NRT for CVD patients, the NHS stop smoking services are now truly established and report an increase in the number of smokers being treated (Department of Health, 2008). In 2004, the Quality and Outcomes Framework was introduced, which provides monetary incentives for GPs to record the smoking status of registered patients and to advise those with specific diseases to stop (Department of Health, 2004). In addition, NICE has provided advice on brief interventions (Stead, McNeill, Shahab, & West, 2005; NICE, 2006). All of these factors are likely to have contributed to a change in the *status quo* of treatment of smokers with diseases and thus makes it likely that the picture regarding the relationship between CVD and smoking and smoking cessation will be different now than it was in 2003.

### **IX.iv.v   Implications and conclusions**

Guidelines on the prevention of cardiovascular diseases development, morbidity and mortality stress the importance of smoking cessation. However, in terms of the primary prevention of cardiovascular disease, data from the Health Survey for England in 2003 show that people at high risk of developing CVD are not being identified at an adequate rate<sup>73</sup>. This is particularly worrying when smokers are even less likely to be diagnosed with a CVD-related disease, hypertensive patients being a case in point. Considering the synergistic effects for CVD risk arising from the combination of smoking with various risk factors (e.g. unhealthy lifestyle, diabetes etc), a greater effort is required to reduce the smoking prevalence among individuals – especially among younger people – displaying such risk factors, who, according to the results, are more likely to be smokers in the first place. However, smokers at greater risk must first be identified before help can be provided to avoid the onset of CVD. A diagnosis with disease has the potential to become a “teachable moment” (McBride, Emmons, & Lipkus, 2003), which may provide an additional impetus for cessation as shown by the example of greater motivation to stop smoking among those reporting a CVD diagnosis and increased smoking cessation among diagnosed hypertensive patients.

In terms of the secondary prevention of cardiovascular diseases, the fact that after adjustment for confounding variables there was no difference in smoking prevalence between those reporting and not reporting a CVD diagnosis emphasises the need for more efforts to reduce cigarette smoking in CVD patients. In the light of this, it is rather disconcerting to see that two out five people with CVD did not recall ever being advised to stop, and that less than a third had been advised within the last year. Indeed, quit

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<sup>73</sup> However, as a caveat, it should be acknowledged that given the changes discussed in IX.iv.iv that this may have improved since.

advice to patients in the UK compares badly to other European countries (see EUROASPIRE II Study Group, 2001), and this study provides further evidence of this.

It is clear that while for some patients advice from a physician will be enough to motivate cessation, for many smokers with CVD or CVD risk factors advice alone may not be sufficient, especially since these smokers appear more dependent. However, there is good evidence that smokers with CVD and CVD-related diseases may be more amenable to interventions than smokers with other diseases or no diseases (see Critchley & Capewell, 2003; John, Meyer *et al.*, 2006) and that more intensive interventions can be very effective in this population (Thomson & Rigotti, 2003). Thus, there is still considerable opportunity to further reduce the burden of cardiovascular disease in England by identifying and specifically targeting smokers with concurrent CVD risk factors or disease in addition to providing tailored quit advice and, where needed, further assistance for smoking cessation to this vulnerable group of people.



## Chapter X

### General Discussion and Conclusions

#### ***X.i Aims***

The aim of this thesis was to broaden our understanding of the role and application of biological markers of smoking-related exposure, risk and harm in tobacco control in general and smoking cessation in particular. In order to achieve this objective, the current thesis used data from both small, experimental (Studies 1 through 3) as well as large, epidemiological (Studies 4 and 5) investigations and supplemented the mainly quantitative approach (Studies 1, 3, 4 and 5) with a qualitative enquiry (Study 2). The use of disparate methodologies, it is hoped, will have increased the scope of what can reliably be concluded about the utility of biomarkers for tobacco control. However, as an off-shot of this approach, it should be noted that owing to the differences in the study methodologies which allowed this PhD to cover a large range of different issues, each of the studies was designed to stand alone as well as to contribute to this thesis as a whole.

As indicated in the introduction, tobacco control can be characterised in terms of the domain of action within which tobacco control is carried out. This comprises strategies based on legislation and policy, on basic research, public awareness and values or on intervention programmes (Slama, 2004). Chapter II already outlined how the various biological indices of smoking-related exposure, risk and harm have contributed to each of these domains of actions so far, and the current thesis aimed to add further evidence for the utility of biomarker feedback in these three areas of tobacco control by investigating the role of biomarkers in five different studies with five different and relevant research agenda pertaining to tobacco control with a specific emphasis on smoking cessation (see Table X.I for an overview).

**Table X.I Study by tobacco control domain matrix**

	Policy and Legislation	Intervention programmes	Basic research, awareness, values
Study 1	✓		
Study 2		✓	
Study 3		✓	
Study 4	✓	✓	✓
Study 5	✓	✓	✓

The first study opened with a broad, preliminary point of interest and examined whether biomarkers of exposure are required at all or could just simply be substituted by self-report. This study explored the potential for replacing biomarkers in policy evaluations of changes in legislation related to the emission of cigarettes and associated alterations in the exposure of smokers. Study 2 moved on to focus on smoking cessation; however, so as to gain a general overview of the area, this exploratory, qualitative study investigated smoking cessation at the individual level by analysing interviews of smokers and ex-smokers to chart their progress towards cessation and, more specifically, to gain insights into their views of the Stop Smoking Services as well as the use of biomarkers in smoking cessation interventions. Following on from Study 2, Study 3 tested the effectiveness of such an intervention using a biomarker of smoking-related exposure and risk. Finally, looking at the broader picture, both Study 4 and 5 assessed the potential value of biological markers of smoking-related risk and harm that are used in the diagnosis of two prevalent diseases associated with premature morbidity and mortality among smokers, COPD and CVD, by evaluating their association with smoking cessation in a population sample. These studies also serve to demonstrate the importance of biomarkers for basic research carried out in tobacco control and their potential to raise awareness of important issues affecting future health care policy.

In what follows, the main findings from this thesis are summarised and their contribution to the extant literature and practice indicated.

### ***X.ii Summary of main findings and contribution to literature and practice***

#### ***X.ii.i Can measures of self-reported puffing replace biomarkers of smoke exposure?***

An obvious starting point for an investigation looking at the utility of biomarkers is to evaluate whether biomarkers are strictly speaking necessary, and Study 1 therefore assessed if self-reported measures of puffing behaviour are equally reliable and valid as actual biomarkers of smoke exposure. The results indicate that self-reported puffing behaviour is stable over time at a comparable level to machine-assessed puffing and that it has some predictive validity in terms of smoke exposure determined at the mouth level, i.e. puffing behaviour assessed by a smoking topography device or by analysis of solanesol and nicotine in spent cigarette butts. However, the results also suggest that self-reported measures do not predict smoke exposure at the level of actual bodily intake as determined by a biomarker of exposure that is usually considered to provide a gold standard, cotinine. This finding is perhaps not surprising considering the many unobservable factors such as nicotine metabolism and lung morphology that influence exposure. Study 1 thus provides evidence that biomarkers of exposure cannot simply be substituted by self-report measures. It highlights the importance of biological markers for the evaluation of legislative changes that are introduced to reduce smokers' exposure to carcinogens (e.g. European Directive 2001/37/EC placing upper limits on emissions) as well as changes in smoking behaviour following a stricter tax policy on cigarettes; self-report is not sufficiently accurate to gauge the effectiveness of legislation and policy changes and exposure biomarkers are therefore essential.

This research expands on earlier studies that have looked at the association between self-report and exposure biomarkers (e.g. Hofer, Nil *et al.*, 1992) both in terms of the

sample size and in terms of the setting as this is the first multi-country study to have investigated the reliability and validity of self-reported puffing behaviour. The present study also helps elucidate previous contradictory findings regarding the relationship between self-reported inhalation and smoking exposure (e.g. Hill, Haley *et al.*, 1983; Nakayama, Yokoyama *et al.*, 1999; Etter & Perneger, 2001) by confirming that self-reported inhalation does not correlate with smoke exposure at the mouth or bodily level and that self-reported smoking intensity does not predict actual smoke exposure.

### **X.ii.ii How do smokers progress towards smoking cessation?**

Before looking at the role of biomarkers in smoking cessation, it is first necessary to better understand the progress towards cessation. As there is a surprising lack of contextualised information on how smokers move from being a smoker to being a non-smoker, this study adapted an exploratory, qualitative approach to look this issue. Study 2 therefore focused on the differences and similarities between smokers who had either attempted to stop smoking or had never attempted to stop smoking and those who had either succeeded or failed to stop smoking to further our understanding of the processes involved in the transit towards smoking cessation.

Most smokers who had never attempted to stop tended to emphasise the positive effects of smoking (enjoyment, stress relief, social aspect) while downplaying the negative effects (addiction, health effects); never quitters implicitly justified their continued smoking by appealing to their rebellious nature, not wanting to succumb to societal norms. However, it was commonly health concerns (rather than pressure from society) that precipitated a change in the attitudes of smokers and demarcated smokers who had attempted to quit from those who had never attempted to stop smoking. Smokers appeared to arrive at the decision to stop following different paths; some smokers put particular emphasis on extrinsic reasons for motivating their quit attempt (such as

stopping smoking for a family member) whereas others primarily cited intrinsic reasons as motivating the quit attempt (e.g. having enough of smoking and addiction). The main factor that seemed to differentiate successful and unsuccessful quitters was an acknowledgement of the need to accept responsibility for one's own behaviour in self-accounts of the former but not the latter group of interviewees. Blaming others and shifting responsibility for continued smoking to a number of external factors was a recurrent theme among those who had failed to stop smoking. In contrast, those who had succeeded recounted that there came a moment when they realised that nobody else could stop for them, and that they themselves would have to accept responsibility for stopping smoking. However, again not everybody who stopped smoking reached this conclusion in the same way; some ex-smokers took a pragmatic stance, acknowledging their former enjoyment of smoking and that the reason for stopping was extrinsically motivated necessity (usually because of current or future health concerns). In juxtaposition to this, some former smokers described how their whole outlook on smoking changed, resulting in an intrinsic shift and not being able to understand their past behaviour as a smoker anymore, *de facto* adopting a new identity as a non-smoker.

Thus results from this study suggest that there are three main syncretic driving forces mediating the path from smoking to smoking cessation: raised awareness, build up of (intrinsic/extrinsic) pressure or motivation to stop, and acceptance of responsibility for own behaviour. While some of these processes have been captured in earlier qualitative work (e.g. Puskar, 1995; Wiltshire, Bancroft *et al.*, 2003), this is the first study of its kind to qualitatively investigate the process of cessation in an English sample. Moreover, this study highlights that there still remain smokers who need to be made aware of the consequences of smoking and that interventions focusing on both extrinsic as well as intrinsic reasons for cessation are useful for increasing awareness and

motivation to stop smoking - though different smokers will differ in their responsiveness depending on the reasons emphasised. Indeed, the results suggest that extrinsic, downward social comparison may be a powerful tool to motivate smokers to attempt and succeed in stopping smoking, an area of research which has received relatively little attention thus far. Lastly, this study adds to previous qualitative studies by underlining the importance of identity to smoking and smoking cessation. More specifically, the self-conception as a rebel may prevent smokers from considering stopping smoking. Yet, in agreement with identity shift theory (Kearney & O'Sullivan, 2003) and Prime Theory (West, 2006b), small successive steps may lead to a 'Eureka' moment and result in an equally pervasive change in identity, yielding a non-smoker who is resistant to return to smoking.

### **X.ii.iii What are smokers' perceptions of existing smoking interventions?**

Study 2 included participants that had either gone through the NHS stop smoking services or had never attended these. This study design provided an opportunity to not only gather suggestions on how the existing services could be improved from an inside perspective (former service users) but also highlight how the services are appraised from the outside perspective and thus recommend ways in which UK Stop Smoking Services can be enhanced to appeal to new users.

Although smokers who had failed in their quit attempt were more likely to comment on the need to teach more specific skills and to have greater flexibility in attitude towards other cessation methods, smokers who had used the Stop Smoking Services were in general very positive about these, irrespective of the success of their attempt, and felt that sufficient information and materials were provided. However, users had a somewhat ambivalent attitude towards the set-up of clinics – while some participants

liked group counselling, others strongly objected to it. It was felt that groups were too large and ensuing waiting times too long. Moreover, smokers who had never been to a stop smoking clinic expressed that one barrier to attending the clinics was their perceived similarity to other rather more stigmatised group-based counselling programmes such as Alcoholics Anonymous. These smokers also felt that access to smoking clinics should be improved as the current restrictions in terms of their opening times and locality may prevent them from coming along to the services.

Only a very small number of studies has looked at service users' views of the smoking cessation clinics and while some of these findings have been previously reported in the literature (e.g. Balch, 1998; Ahijevych, Kuun *et al.*, 2003; Amos, Wiltshire *et al.*, 2006), this study provided additional insights. In contrast to earlier studies using different population samples (Vuckovic, Polen *et al.*, 2003; Kishchuk, Tremblay *et al.*, 2004), characteristics of counsellors and treatment of smokers did not feature as a great concern. Rather, this study emphasises that although some successful quitters may appreciate the competitive aspects of groups, others will find a smaller setting to share their experiences more helpful. Findings also suggest that there is a need to correct people's perception of the Stop Smoking Services as something akin to clinics for heavy drug users by, for instance, making potential users aware of the differences in the set-up (e.g. choice of both individual and group counselling). Lastly, results imply that improving the access to clinics further will increase attendance of those currently not considering Stop Smoking Services as an option.

### **X.ii.iv What are smokers' views on the use of biomarkers in smoking interventions?**

Study 2 lastly probed participants' views on the use of biological markers in smoking cessation interventions and found that the overwhelming majority of smokers and ex-

smokers welcomed the addition of biomarker feedback to existing interventions. Indeed, a number of current and former smokers who had attended the Stop Smoking Services felt that weekly feedback of expired air-carbon monoxide readings was one particularly useful aspect of the clinics as this individualised the treatment and this study highlights the utility of biomarkers in existing intervention programmes. However, participants also felt that - as in any fear appeal - the right balance would need to be struck when utilising biomarkers since, depending on the outcome, feedback may on the one hand alienate and terrify and on the other hand reassure smokers to continue. Thus appropriate additional support would need to be provided in such interventions.

A number of qualitative studies have previously looked at the use of fear appeals in smoking cessation (e.g. Butler, Pill *et al.*, 1998; Foraker, Patten *et al.*, 2005), but this is the first study to look at the application of biomarkers specifically. The results imply that smokers and ex-smokers consider the application of biomarkers in smoking cessation interventions generally as justified. In particular, it appears that something as simple and easy as expired CO feedback may prove viable since it personalises risk and enables smokers to see an improvement (reduction in CO levels) after successful behaviour change thereby motivating continued cessation.

### **X.ii.v Does biomarker feedback impact on cognitive antecedents of behaviour change?**

Following on from Study 2, Study 3 sought to evaluate not only whether biomarker feedback is effective at increasing quit rates (see X.ii.vi) but also to investigate possible pathways that explain the potential impact of biomarker feedback on cessation by looking at constructs derived from fear appeal and cognitive process models: the Extended Parallel Processing Model (Witte, 1992) and emotional processing theory (Rachman, 1980). The biomarker used in this intervention, expired air carbon-



monoxide, was chosen on the basis of the outcomes from Study 2. In line with theoretical predictions, results of this randomised controlled trial showed that carbon-monoxide feedback increased perceived susceptibility levels compared with the control group, underlining the efficacy of biomarker feedback to undermine optimistic bias through the presentation of evidence of actual smoking-related exposure, risk or harm. Contrary to expectations, fear levels were not raised in the treatment group in comparison with the control group but as postulated by the fear appeal model, susceptibility and fear levels interacted with self-efficacy; only among those with low self-efficacy was increased susceptibility associated with increased fear. Moreover, as expected, carbon-monoxide feedback increased motivation to stop smoking in the treatment relative to the control group. However, this difference in motivation levels was short-lived and had dissipated after six months.

This study is one of the first to apply general cognitive and fear appeal models to investigate the impact of biomarker feedback on cognitive antecedents of behaviour change. It improves on previous studies in terms of sample size (Shahab, Hall *et al.*, 2007) and comprehensiveness of the measures included (Bishop, Marteau *et al.*, 2005). Although biomarker feedback had an impact in the expected direction on some of the postulated cognitive antecedents, this study was able to confirm predictions from these models only to some extent.

### **X.ii.vi Can a simple intervention involving biomarker feedback increase smoking cessation rates?**

The provision of carbon-monoxide feedback in Study 3 did not increase any of the behavioural outcomes compared with the control condition; smokers in the treatment group were not more likely to attempt to stop smoking, to have stopped smoking or to have engaged in any other smoking cessation behaviour. However, self-efficacy level

interacted with group allocation on smoking cessation; the effect of the intervention was restricted only to participant with high self-efficacy levels and among those with elevated self-efficacy, it resulted in an increased likelihood to have stopped smoking compared with the control condition. The limited impact of the intervention on behavioural outcomes is likely to stem from the high degree of matching between the treatment and control conditions and the relatively minimal level of intervention in this study. Moreover, the study sample was not selected on the basis of their motivation to stop smoking. Altogether these factors may have depressed the impact of biomarker feedback on cessation and this study provides partial evidence for the utility of biological markers for smoking cessation programmes.

These results confirm those from earlier studies using a comparable set-up (Jamrozik, Vessey, Fowler, Wald *et al.*, 1984; Sanders, Fowler, Mant, Fuller *et al.*, 1989; Audrain, Boyd, Roth, Main *et al.*, 1997; see Chapter III for details) and underline that this type of exposure feedback may have rather limited potential to increase engagement in smoking cessation behaviours and should be restricted to highly motivated smokers. However, this study improves on previous studies of CO feedback by also considering the impact of self-efficacy on outcome and suggests that this type of intervention may be particularly useful not only for smokers that are already motivated but also smokers who display a higher level of confidence (self-efficacy) in their own ability to quit, an effect which has also been observed in studies of other biomarkers (e.g. Shahab, Hall *et al.*, 2007).

### **X.ii.vii What is the prevalence and level of under-diagnosis of biomarker-defined COPD in England?**

Study 4 used data from the Health Survey for England for an epidemiological investigation of COPD prevalence and diagnosis in England. Results revealed that

COPD as defined by a biomarker (spirometry) is relatively common in the English population; more than one in eight people above 35 years of age displayed signs of this syndrome. Perhaps even more worrying was the degree of under-diagnosis of COPD in the population, as only one fifth of people with objective signs of the syndrome reported a diagnosis with any respiratory disease and even among people with severe forms of COPD, only half indicated a diagnosis. These results were stable irrespective of the definition of COPD that was used in the analysis. This study thus provides evidence for the importance of biological markers for raising awareness of overlooked issues in smoking research in order to draw greater public attention and indicate potential areas for policy changes. Indeed, in response to the published study, a report was commissioned by the British Lung Foundation to highlight the large level of underdiagnosis of COPD in England.

This is the first study to provide national prevalence estimates for objective COPD in England using a commonly used biomarker of smoking-related harm, spirometry. This study is also the first to report the population-wide level of under-diagnosis of this syndrome in England. Findings from Study 4 are comparable to epidemiological data from other countries both in terms of prevalence (Mannino & Buist, 2007) and diagnosis (Mannino, 2006) and underline the magnitude of the problem that COPD presents in England.

### **X.ii.viii What is the smoking prevalence among people with COPD?**

As there exists a strong causal link between COPD and smoking, Study 4 also looked at the level of smoking among people with biomarker-determined COPD in order to estimate the extent to which smoking is an issue in this population and to determine the level of resources that need to be put into place to tackle it. The results show that smoking in this vulnerable group is a real problem as over a third of people with the

disease - significantly more than without it - smoked and this holds true across all age groups. Indeed, nearly half of people with spirometry-defined COPD in middle age were current smokers and again this study shows how biomarkers can raise awareness of important, yet overlooked, issues in tobacco control.

While the incidence and prevalence of COPD among smokers is well recorded (e.g. Fletcher, Peto *et al.*, 1976), Study 4 is the first of its kind to provide estimates of the converse – the smoking prevalence among people with biomarker-defined COPD in a nationally representative sample. Considering that smoking cessation is currently the only viable option to appreciably slow the progression of COPD once developed, the results suggest that more resources and effort are needed in secondary prevention to help smokers who have developed objective signs of COPD to stop smoking.

### **X.ii.ix Does a diagnosis with a respiratory disease increase smoking cessation rates?**

Lastly, and most pertinent to the remit of this thesis, Study 4 also assessed the extent to which a disease diagnosis impacts on smoking cessation rates in order to evaluate the role of smoking-related biomarkers of harm such as spirometry in this particular context. Bearing in mind that data come from a cross-sectional survey with obvious limitations regarding the direction of effects and potential confounding (as discussed in VIII.iv.i), the results in the very least are consistent with an interpretation suggesting that a diagnosis with a disease can elevate the motivation to quit of smokers who have COPD. However, since these smokers were also found to be more dependent than smokers with impaired lung function, this increase in motivation did not translate into higher quit rates.

Spirometry alone is thus unlikely to increase cessation and this is in agreement with the outcome of interventions using lung function tests that were reviewed in Chapter III (e.g. Segnan, Ponti, Battista, Senore *et al.*, 1991). However, considering the large burden of COPD on smoking-related morbidity and mortality, this study provides first evidence that routine spirometric assessment can fulfil a double function – to both identify smokers with COPD in need of attention and to provide a basic impetus towards smoking cessation. Indeed, as shown by the Lung Health study (e.g. Kanner, Connett *et al.*, 1999), this initial motivation can be converted into abstinence given the right level of support.

### **X.ii.x What is the prevalence and level of under-diagnosis of biomarker-defined CVD and CVD risk factors in England?**

The Health Survey for England in 2003 focused on cardiovascular disease and Study 5 used data from this survey to evaluate the prevalence of CVD and CVD risk factors in England. CVD based on self-report was common in the population; over one in seven participants said they had been diagnosed with some form of CVD. The prevalence of people with a high or very high risk of heart disease as defined by biomarkers was very similar at around 13%. Of the behavioural CVD risk factors considered, inadequate vegetable and fruit consumption as well as physical inactivity were most prevalent and among biomarkers of CVD-risk elevated C-reactive protein counts and high blood pressure readings were most common in this sample.

In terms of the detection of CVD and CVD risk factors, Study 5 showed that only about a fifth of people with the highest risk of heart disease reported a diagnosis with any CVD. In terms of the diagnosis of CVD-related diseases, biomarker-determined diabetes had poorest detection rates (~50%) while both objectively defined hypertension (~70%) and metabolic syndrome (~80%) had good levels of detection. However, the

analysis also revealed that smokers were not more likely to be diagnosed with any of the diseases but rather – as in the case of hypertension – less likely to receive a diagnosis. This study, as study 4, thus highlights an area in the treatment of smokers that needs to be looked at in greater details, possibly requiring changes in the policy approach to the diagnosis of hypertension in primary care. The biological markers of harm used in this study allowed for an objective diagnosis of hypertension and thus enabled the detection of a pertinent problem for smokers with the aim of raising awareness of this issue.

Prevalence data from this analysis corroborate results from earlier studies looking at CVD (e.g. Strong, Maheswaran *et al.*, 2006) and CVD risk factor prevalence (e.g. Ajani, Ford *et al.*, 2006). This is the first study in England to provide a population estimate of the detection of individuals at high risk of heart disease and one of only very few studies from around the world to estimate the detection of other CVD-related diseases such as diabetes at population level (e.g. Faeh, William *et al.*, 2007). These results underscore not only how widespread cardiovascular disease and associated risk factors are in England but also imply that there is need for better detection of CVD and CVD risk factors among high-risk individuals, i.e. smokers.

### **X.ii.xi What is the smoking prevalence among people with CVD or CVD risk factors?**

As in the case of COPD relatively more is known about the prevalence of CVD and CVD risk factors among smokers than about the smoking prevalence among people with CVD and CVD risk factors. In contrast to the findings in Study 4, the smoking prevalence for people reporting or not reporting a CVD diagnosis was very similar after controlling for possible confounders. However, people with CVD, as those with COPD, were more nicotine dependent. Smoking prevalence for people with and without CVD-related diseases were equally similar and only lower among those with hypertension.

Considering the causal relationship between various inflammatory and neuroendocrine markers and smoking, it comes as no surprise that smoking prevalence among people with elevated biomarkers of CVD risk was significantly higher than among those with normal levels. Lastly, with regard to behavioural risk factor, this study revealed a clustering of unhealthy life-styles; that is, smoking prevalence was higher among those with high alcohol and low vegetable and fruit consumption.

Results from Study 5 help clarify some contradictory findings in the literature regarding smoking prevalence among hypertensives (e.g. see Hunt, Hopton *et al.*, 1990; Nothwehr, Elmer *et al.*, 1994) and those with the metabolic syndrome (e.g. see Park, Zhu *et al.*, 2003; Ford, 2005), indicating significantly lower smoking rates only in the former and not latter group. This study is also one of just a handful of studies which have looked at the smoking prevalence among people with CVD and IHD (e.g. EUROASPIRE II Study Group, 2001) and highlights that although smoking rates in this group compare favourably with those of CVD and IHD patients from other countries, it has remained at high levels for people with CVD risk factors. In light of the synergistic effects that smoking and these risk factors have on the subsequent development of CVD, this draws attention to the continued need to reduce smoking in this vulnerable group.

### **X.ii.xii Does a diagnosis with CVD or CVD risk factors increase smoking cessation rates?**

The last question addressed by Study 5 returns to the issue of the impact of a diagnosis with biomarker-determined disease on smoking cessation. Again, it is important to remember that data come from a cross-sectional survey and thus conclusions derived from these data carry certain caveats (see IX.iv.iv). Encouragingly, smokers who reported a diagnosis with CVD were more likely to have been advised to stop than

smokers without reported CVD and the results are consistent with the finding that smokers with CVD were more motivated to stop smoking than those without self-reported CVD. Among smokers with biomarker-defined CVD-related diseases, those with a diagnosis were more likely to report having received quit advice – at least in the case of hypertension and the metabolic syndrome. Yet, among those with objective signs of disease, a diagnosis was not associated with an increase in their motivation to stop smoking. However, there was a positive association between receiving quit advice and smoking cessation. Smokers who according to their blood pressure results were hypertensives and reported a diagnosis with hypertension were significantly more likely to have stopped smoking than smokers with hypertension who were unaware of the disease. The picture was somewhat similar with regards to diabetes but the impact of receiving a diagnosis did not reach significance. In contrast, there was no discernable difference in quit rates between smokers with and without the metabolic syndrome as a function of reporting a CVD diagnosis.

This is the first study in England to specifically evaluate the impact of a disease diagnosis on smoking cessation among people with biomarker-verified signs of cardiovascular diseases. This study also contributes to the general literature on the prevalence and effect of the provision of quit advice for smokers with diseases (e.g. Novotny, Fiore *et al.*, 1990; Maguire, Ryan *et al.*, 2000; Wallace, Sairafi *et al.*, 2006). While those with diseases were more likely to receive advice, the results also confirm that despite ever growing evidence for the smoking-disease link, the rate at which quit advice is offered has not increased over the last twenty years. Moreover, this study highlights the ‘double-whammy’ of the failure to detect smokers with the CVD-related diseases. Not only are they less likely to receive stop smoking advice than their peers, in the case of hypertension (and tentatively diabetes) they are also less likely to have



stopped smoking. These findings suggest there yet exist considerable opportunities to reduce the burden of smoking-related CVD through an improvement in both primary and secondary prevention using biomarkers to identify those at risk or with disease and motivate smoking cessation.

### ***X.iii Limitations***

The studies in this thesis have drawn on the strength of using diverse methodologies to elucidate the role and application of smoking-related biomarkers of exposure, risk and harm and, as described above, have been able to make a number of interesting and worthwhile contributions to literature and practice. However, it is inescapable that this type of research is also subject to a few limitations. Most of these have been discussed in the relevant chapters, but some important general limitations are acknowledged here.

#### ***X.iii.i Representativeness and sampling***

Population representativeness is a perennial problem in research as only relatively large samples provide enough differentiation in terms of the socio-demographic profile of participants to be truly representative of the population, which means that strictly speaking most research findings cannot be generalised beyond the immediate sample. For this reason, appropriate sampling frameworks are required to ensure the representativeness of included participants. However, owing to its idiographic stance, this issue is less relevant for qualitative research. Indeed, the purposive sampling strategy in Study 2 meant that participants were not randomly selected but deliberately chosen to fit into three categories. The limitations that this poses for qualitative studies in general are reviewed in more detail in Chapter VI and findings from Study 2 have to be viewed in this light. Representativeness is also less of a problem in Studies 4 and 5 as both were based on data from a large household survey that used a multi-stage, stratified probability sampling design to be representative of the English population. In

contrast, neither Study 1 nor 3 used a specific sampling design to ensure representativeness but rather opportunistically recruited smokers into the studies. As a result, both studies somewhat over-sampled men and younger smokers. In addition, the sample in Study 3 was relatively more affluent compared with the latest General Household Survey data on the smoking population in England and Wales (Goddard, 2006). Unfortunately, ethnicity was not assessed in either study and ethnic representativeness of the samples could therefore not be evaluated.

### **X.iii.ii Design and measurement**

The various study designs employed in this thesis have important implications for the interpretation of results. Both large-scale studies (4 and 5) were cross-sectional thus conclusions regarding causal relationships that are presented have to remain completely speculative. In addition, the cross-sectional nature of the surveys introduces the potential for recall bias – at least for self-report measures such as doctor diagnosis – which may have confounded results. Moreover, as an objective biomarker of smoke exposure (cotinine) was collected only from a sub-sample in Study 5, it is possible that smoking prevalence in this sample was underestimated.

As opposed to Studies 4 and 5, the two remaining quantitative enquiries used a longitudinal design. However, in the case of Study 1, the set-up of the study may have influenced results as participants were required to smoke cigarettes through a smoking topography device, which could have altered the sample's smoking behaviour and this therefore limits the conclusions regarding self-report and 'typical' puffing behaviour in this study. The other longitudinal investigation, Study 3, would have benefited from an additional minimal control group in which participants would not have received either biomarker feedback or a leaflet. This would have improved on the before-after approach taken in the evaluation of the impact of the leaflet on cognitive outcomes as it currently

cannot be precluded that changes over time were due to other intervening, unmeasured factors. Moreover, owing to pecuniar and logistic restrictions, smoking cessation was not biochemically verified in this study, which may mean that self-reported abstinence in this sample was overestimated. Lastly, both Study 1 and 3 suffer from having relatively small sample sizes and therefore rather limited power to detect all relevant statistically significant differences and associations. However, while this may have had an impact on the detection of more subtle effects, the studies were powered to test main hypotheses and thus findings based on these larger effects can be considered robust.

### **X.iii.iii Data analysis**

Before turning to issues of the quantitative analysis, I shall briefly consider those related to the qualitative analysis carried out in Chapter V. Although safeguards were put in place to ensure that results derived from this analytical technique were reliable and valid, it is impossible to exclude the possibility of personal biases impacting on the interpretation. To eradicate such bias completely would require a meta-interpretation of my interpretation by other researchers, whose views in turn would need to be interpreted by other researchers to eliminate subsequent bias; a regress that could continue *ad infinitum*. For this reason, it is important to remain aware of this inherent drawback of qualitative research<sup>74</sup>.

Much care was taken throughout this thesis to test for statistical assumptions regarding the normality and spread of data that were analysed. However, in this analysis a perhaps controversial stance on the treatment of Likert responses was taken. Responses on Likert-type scales strictly speaking should be analysed with non-parametric tests because they cannot be considered continuous in the same way as data derived from

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<sup>74</sup> However, some would argue that similar problems also apply to quantitative research (e.g. see Whittemore, Chase, & Mandle, 2001)

interval or ratio scales with equivalent intervals and/or true zero values (Kuzon, Jr., Urbanchek, & McCabe, 1996). Despite this objection, Likert responses were treated as interval scale responses in the analysis. This is not uncommon and there is an argument that Likert responses can be considered appropriate for parametric tests given normality in distribution and an appropriate sample size (e.g. Knapp, 1990). Nonetheless, it needs to be acknowledged that some of the longitudinal analyses in this thesis may have been compromised by an observed lack of variation in dependent Likert-based variables. Another, related point is that most statistical techniques such as multiple regressions are affected by the quality and accuracy of the measures used such that an observed association, or lack thereof, may be a result of one variable being measured relatively better than another. This problem was minimised in this thesis by using measures that were previously validated but as this was not possible in Study 1, it may have influenced these results. Lastly, missing data can introduce bias and for this reason, where possible, participants with missing data were considered separately to evaluate systematic differences between those included in the analysis and those not.

### **X.iii.iv Scope of the research**

A final limitation to consider is the trade-off between detailed analysis and the scope of this thesis. As was outlined in the first few chapters, there exist a plethora of smoking-related biological markers and with continuous advances in biomedical research, the number of biomarkers is likely to increase further. This thesis was therefore able to consider only a small fraction of these and while an attempt was made to include at least one of each type of smoking-related exposure, risk and harm biomarker, better and more suitable biomarkers may have been, or become, available. Arguably, the number of biomarkers is as great as the number of possible applications for them. In order to meaningfully investigate this broad area of research and to increase consistency between studies, I therefore made the decision to focus primarily on the role of

biomarkers in smoking cessation for the sake of coherence. Yet, as indicated in Chapter II, biomarkers have been applied in many other areas of tobacco control. For instance, there is a growing interest in the use of biomarkers in product regulation. Biomarkers can help determine human exposure to various carcinogens that are present in tobacco smoke with a long-term view to curtail exposure in humans by imposing upper limits on the concentrations of carcinogens that are delivered by each cigarette. Unfortunately, this important and interesting application of biomarkers could not be considered in this thesis. However, even within the more limited scope of a thesis that looks at the role and application of a small number of biomarkers in smoking cessation, there still remains too much to cover to investigate every angle of this topic. Thus, this thesis did not specifically consider the differential impact of biomarker feedback in sub-groups such as younger or more deprived smokers; likewise there was no opportunity to assess the role of biomarkers of genetic risk for smoking-related diseases such as lung cancer (another research area that is becoming increasingly popular) or the potential use of personalised biomarkers in more interactive media such as in mobile phone or internet based intervention. However, I hope the studies that have been included will have added to this research area, elucidated some hitherto overlooked issues and be valuable for the conception and development of prospective enquiries.

### ***X.iv Future research***

The findings from the studies included in this thesis have implications for practice and theory and thus future research. Study 1 has shown that self-reported puffing does not predict biomarker-determined exposure to smoke intake. However, more research is needed to evaluate whether self-reported measures with better sensitivity can be developed in order to reliably and validly capture actual intake among smokers. Moreover, it would also be worthwhile to investigate self-reported puffing behaviour in a natural setting with longer follow-up times to assess the sensitivity of self-report to

changes over time. Research in this area is important as tobacco companies increasingly shift towards globalised strategies and policies. These include the manipulation of cigarette design to circumvent product regulation in a given country, the 10-1-10 policy in Europe is a case in point (for more details see O'Connor, Cummings, Giovino, McNeill *et al.*, 2006). For this reason valid, reliable self-report measures of smoke intake will become ever more crucial for the study of such changes at the population level where the use of exposure biomarkers would not be feasible.

It is in the nature of qualitative work that its results may pose more questions than they answer, and this is also true for Study 2. While there were some discernable differences between smokers having attempted and not attempted to stop or smokers having succeeded and not succeeded to quit, it is less clear how smokers can be moved along the path towards cessation. Future research could, for instance, evaluate the potential of behavioural experiments that raise smokers' awareness. In this study, many smokers who had never attempted to stop denied being addicted to nicotine and therefore also doubted the utility of nicotine replacement therapies. Asking smokers to abstain from smoking for a given period may help initiate a shift in smokers' perception of their own vulnerability to addiction and thus motivate them to take further steps towards considering cessation.

Future research should also look at the role of social comparison in smoking cessation interventions. One of the upshots of the results in this study is that smokers who thrive on competition may do better in group settings than smokers who are internally motivated to stop smoking and thus would perhaps benefit from individual therapy. The potential of identifying these types of smokers and subsequent tailoring of smoking cessation interventions towards their needs is something that may be worthwhile to

investigate in future studies. Lastly, results suggest that increasing access to and overcoming stigmatisation of the UK Stop Smoking Services could increase up-take by potential users. Although there may currently not exist a wish to increase attendance, it could be speculated that those most in need of support are missing out because of these barriers. Thus, future research could, as, indeed, is already happening, look at the utility of providing work-based Stop Smoking Services or local media campaigns to both improve access to as well as the image of the services among potential users.

One of the research questions derived from Study 2 and assessed in Study 3 was whether carbon-monoxide feedback added to brief advice would increase smoking cessation rates. The findings suggest that this intervention was only effective for a subgroup of smokers, those with high self-efficacy, and future research should investigate whether this finding generalises to other types of interventions and, if so, whether there exist viable ways to increase the self-efficacy levels of smokers. In addition, as argued in Chapter VII, future research should also consider visual biomarkers of smoking-related harm as interventions employing harm biomarkers may prove more effective than exposure or risk biomarkers in changing health behaviours. Unfortunately, this study was underpowered to assess causal pathways mediating the impact of feedback on smoking cessation. It would seem that the pathways postulated by the Extended Parallel Processing Model and emotional processing theory in particular deserve more attention. For instance, emotional processing would predict that the efficacy of different types of biomarkers (e.g. exposure vs. harm biomarker) derive from their ability to access fear networks, which would favour the use of visual harm biomarkers over other biomarkers. Using appropriate measures of arousal (e.g. blood pressure or adrenaline) this hypothesis could be tested by relating increased biological arousal during the intervention to subsequent cessation.

Study 4 has raised a number of issues that will need to be addressed and are of relevance to the National Service Framework for COPD, which is currently being drafted. Considering the unacceptably high level of under-diagnosis of COPD in England, studies should evaluate not only the feasibility of introducing spirometry screening for at-risk groups (e.g. middle-aged smokers) in primary care but also the effectiveness of screening in this setting to motivate smokers to stop. Regarding secondary care, future research should also confirm whether smokers with the disease are more likely to mislead clinicians about their true smoking status as this will have implications for the treatment of patients. Lastly, considering the low awareness of the disease in the population, a quasi-experimental study of a local or national health promotion campaign to increase knowledge of COPD in the population would be desirable. This allows for the assessment of whether such campaigns are effective in reducing the number of undiagnosed smokers with COPD by increasing the rate at which smokers with symptoms present to their doctor.

The findings in Study 5 raise various questions that require further investigations, especially with regard to the relationship between hypertension, its diagnosis and smoking cessation. Owing to the cross-sectional design of the survey, the potential of recall bias and the somewhat complicated interaction between smoking and blood pressure, it is currently not entirely clear whether there is an association between smoking cessation and diagnosis among people with hypertension because the diagnosis motivates cessation or because smoking cessation exacerbates hypertension thus leading to a diagnosis<sup>75</sup>. Similarly, it is yet uncertain if more smokers with hypertension are missed because smoking masks hypertension or because a diagnosis with hypertension

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<sup>75</sup> However, as indicated in Chapter IX, recent evidence would suggest the latter to be less likely



makes smokers stop. Future research can use longitudinal and observational studies to help elucidate these issues.

Another concern raised by Study 5 is the disappointingly low rate at which quit advice is provided by health professionals. However, since data for this study were collected, the Quality and Outcomes Framework (QOF) was introduced in the UK rewarding GPs for recording the smoking status of and providing quit advice to smokers with CVD. For this reason it would be sensible to conduct a follow-up study to assess changes in the provision of quit advice by health professionals and to evaluate the impact of QOF on actual practice. Finally, in light of the clustering of multiple CVD risk factors, future research may want to revisit the use of interventions that simultaneously target several health behaviours. Although such interventions are likely to be expensive and time-consuming and perhaps less effective for individual behaviours, the net benefit of changing an unhealthy life-style could outweigh these costs and make the development of such a multi-level intervention a prudent venture for the future.

A last, interesting general issue for research investigating the use of biomarkers in smoking cessation relates to their application in particular subgroups of smokers. As indicated in the previous section, this thesis was unable to discern in great detail the differential impact of biomarker feedback in different populations. However, findings from the systematic review would suggest that special groups, such as pregnant women or those with a lower socio-economic status and less education, may benefit relatively more from interventions that are based on biomarkers than more educated, less motivated individuals. This contention requires further examination, especially since improving cessation rates in these groups could be an important step for reducing health inequalities.

### ***X.v Final remarks***

This thesis evaluated the role of smoking-related biomarkers in smoking cessation by assessing their utility over and above self-report in determining smoke exposure, gauging responses of smokers regarding their acceptability, testing their impact in a smoking cessation intervention and appraising their function in identifying smoking-related diseases and motivating cessation in at-risk populations. There is no doubt that smoking-related biomarkers of exposure, risk and harm have been instrumental in all areas of tobacco control: in the evaluation of smoking-related legislation and policy, for raising awareness of pertinent problem in the health care of smokers and for improving intervention programmes. Hopefully this thesis has contributed to the existing literature in highlighting a few of the many useful current and potential applications that biomarkers have for tobacco control and smoking cessation research in particular.

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## APPENDICES

### Chapter III

#### Appendix III.I Data Extraction Sheet

<b>1.) Identification:</b>						
Author						
Article Title						
<b>2.) Population Characteristics:</b>						
Target Population						
Inclusion criteria						
Exclusion criteria						
Recruitment Procedure						
Characteristics of participants:						
Age	Ethnicity	Education	Sex	Geographical Region	Smoking Behaviour	Other
Number of participants in each condition: A B C						
Were intervention and control groups comparable?						
Was the assignment to treatment groups really random?						
<b>3.) Interventions:</b>						
Content of Intervention and/or Control group						
A		B		C		
Intervention site						
Duration of Intervention: A B C						
Delivery Mode of Intervention: A B C						
Who provided intervention? A B C						
Where they trained?						
What moderating variables were investigated?						
<b>4.) Outcomes, outcome measures:</b>						
What was measured at baseline?						

What was measured after the intervention?				
Who carried out the measurement?				
What was the measurement tool?				
Was the measurement tool validated/how?				
How was the validity of self reported behaviour maximised?				
Was the outcome assessor blinded to treatment allocation?				
Time interval between first and second measurement:				
Time interval between first and last measurement:				
<b>5.) Analysis</b>				
Statistical techniques used				
Does the technique adjust for confounding?				
Attrition rate (overall):				
Was attrition explained & how:				
Intention to treat analysis?	Dealing with missing values?	Loss to follow up?		
Number/Percentage followed up form each condition:				
A	B	C		
Results for Primary Outcomes:				
	Condition A	Condition B	Condition C	Control
Var 1: PreTest PostTest Difference				
Var 2: PreTest PostTest Difference				
Var 3: PreTest PostTest Difference				
Effect of the intervention on other moderating variables:				
Var1:	Var2:	Var3:	Var4:	

## Chapter V

### Appendix V.I Ethical approval letter



Department of Psychology

**UNIVERSITY COLLEGE LONDON**

GOWER STREET, LONDON WC1E 6BT

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Professor Robert West,  
Cancer Research UK Health Behaviour Unit,  
Department of Epidemiology and Public Health,  
UCL

20th July, 2004

Dear Professor West,

Thanks for your enquiry concerning a matter of research ethics.

UCL ethical policy with respect to involvement in research led by a scientist from another institution is as follows:

“If UCL staff, and/or UCL students under the supervision of UCL staff, are involved as co-researchers in a project led by a principal researcher from another institution and ethics approval has been granted by that other institution, it is NOT necessary to obtain additional ethics approval from the UCL Ethics Committee.”

Hence, UCL “defers to the CDC Institutional Review Board/Ethics Committee for human subject protection”.

Thus, as a co-investigator on a project being run by the US Center for Disease Control, you will be covered by the decisions of the CDC Ethics Committee.

Yours sincerely,

Mr. Richard E. Rawles

Vice-Chair, UCL Committee on the Ethics of Non-NHS Human Research  
Visiting Professor, University of St. Petersburg

cc Mrs Helen Dougal,

Secretary, UCL Committee on the Ethics of Non-NHS Human Research

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**Appendix V.II Informed Consent Form****1. PURPOSE OF THIS RESEARCH STUDY**

We are asking you to be part of a research study to measure chemicals in cigarettes that get in your body when you smoke. We are doing this study with smokers in four countries - Canada the United States, the United Kingdom, and Australia. We want to know if people who smoke cigarettes with higher amounts of chemicals called tobacco specific nitrosamines (TSNAs) have higher amounts of TSNAs in their bodies. This study will help us answer this question. Everyone in this study will smoke the cigarettes they usually smoke. We will not ask you to smoke any other type or brand.

We will measure the amount of chemicals from cigarettes in your saliva, urine and breath and compare these to the amounts of the same chemicals in the smoke from your cigarettes. We will need to know how much you smoke so we want you to collect all of your cigarette butts for a day and we will have you smoke two cigarettes through a device that measures how you smoke.

If you are a woman, and there is any chance that you may be pregnant, you cannot be in this study. About 100 people will be in the study. The study is sponsored by the U.S. Centers for Disease Control and Prevention, Roswell Park Cancer Institute, The VicHealth Centre for Tobacco Control, the University of Waterloo, and University College London.

**2. PROCEDURES**

If you are in this study, we will ask you to visit the laboratory two days in a row. Both visits to the laboratory will be in the evening to try to make it easier for you to come.

First Visit. During the first visit, we will ask you questions to find out if you are eligible for the study and to find out about your smoking history. If you are eligible for the study, we will ask to see a pack of your cigarettes so that we can know what you smoke.

First, we will give you a small piece of cotton to put in your mouth until it is soaked with your saliva. After you put the cotton into a special container, we will then ask you to go to the bathroom and provide a urine sample. We will send these samples to a laboratory to find out what chemicals from cigarette smoke are in your body.

Next we will test how much carbon monoxide (CO) is in your breath. You will take a deep breath, hold it for 15 to 20 seconds, and then blow into a machine that measures the CO in your breath. After testing your breath, we will have you smoke one of your cigarettes with a special cigarette holder. The cigarette holder will be hooked up to a computer that measures how you smoke your cigarettes. After you smoke the cigarette, we will test the CO in your breath again.

Then we will tell you how to collect your cigarette butts and give you a container to store the butts in. It is important that you smoke only the cigarettes that you normally smoke, but you can smoke as many as you normally would.

You will schedule a time to come back the next day.

On the next day, you will come back to the laboratory, bringing your collection of butts with you, for visit two.

Second Visit. We will ask you about how you smoked during the time between visits. Then you will do the same things you did at the first visit. You will give us a saliva and urine sample. You'll do the CO test, smoke a cigarette with the special holder and do the CO test again.

You will spend from 30 minutes to an hour at each laboratory visit. The total time of your participation in the study will be a little more than one day.

### **3. POSSIBLE BENEFITS**

We don't think that being in this study will benefit you directly, but we think that some people taking part in this study will find it interesting.

We will give you the results of your carbon monoxide levels at the end of the study. We'll also send you the name of a contact person who will be able to answer any questions you may have.

In our other studies some people decided to try to quit smoking after they saw the results of their lab tests. If you want to quit at any time during this study, we will give you information about how to quit and a list of local organizations that provide services to help you quit. However, the decision to use these services and referrals is yours. You don't have to think about or discuss quitting to be in this study. We ask that you inform us if you are going to quit so that we can give you information that may help you quit.

If you want you can get the final results of the study. If you want the final report, we will keep your contact address in a separate file so we can send you the report. We will give you a stamped, addressed postcard that you can send to us if you move so we have your correct address.

Other people may benefit from this study. For instance, if the study finds that certain cigarettes cause smokers to get more dangerous chemicals in their bodies, warnings can be given to people who smoke these cigarettes or who are thinking of starting to smoke.

### **4. POSSIBLE RISKS OR DISCOMFORT**

The risks of taking part in this study are the same risks that you have every day as a smoker. There is no risk in using the device that tests how you smoke. It is like smoking your cigarette with a cigarette holder attached. There are no risks to giving a urine sample. Putting the cotton in your mouth is not risky as long as you do not swallow it. Breathing into the device to measure carbon monoxide has no risk.

It may not be convenient to come to the laboratory when you are scheduled. We will do everything we can to meet your schedule. We will schedule visits for the evening to make it easier for you.

It may be hard for you to save all of your cigarette butts. Saving the butts may require you to change some habits. We will try to make this as easy as possible by giving you a small container that can fit into a pocket or purse to use if you go out in public. It is

important to our study that you not throw butts away, and not put them out by dipping them in any liquid. You should not be in this study if you think this will be too hard to do.

We will tell you of any new information developed during the study that may affect your willingness to continue in the study.

## 5. OWNERSHIP AND DOCUMENTATION OF YOUR URINE AND SALIVA SAMPLES, AND YOUR COLLECTED CIGARETTE BUTTS

The urine and saliva samples and the cigarette butts that we collect during the study will be sent to the lab for testing. The samples will be the property of the scientists doing the study. The samples will be labeled only with your study ID number in order to protect your privacy.

## 6. FINANCIAL CONSIDERATIONS

If you complete the entire study, we will pay you £30 for your time and inconvenience. The compensation is explained below.

(i) Activity	Total
Complete Visit 1	
Includes smoking topography test	£ 6
Urine and saliva specimens	£ 4
At the end of Visit 1	£10
Complete Visit 2	
Includes returning cigarette butts collected over the previous 24 hours, smoking topography test, and questionnaire	£16
Urine and saliva specimens	£ 4
At the end of Visit 2	£20
TOTAL	£30

We may also pay you for your travel costs to the laboratory.

## 7. CONFIDENTIALITY

We will keep the information about you as private as the law allows. We will not use your name or other information that could identify you in any reports, presentations, or scientific articles we write about this study. We may share the information about your participation with the ethics committees that oversee this study to make sure the people who are part of the study are treated fairly.

All of the information and specimens that you give us will only have a number on them not your name. The file that links your name with the number will be kept in a separate

locked file. We will destroy the information with your name on it when the study is finished.

## 8. TERMINATION OF RESEARCH STUDY

You are free to choose whether or not to be in this study. You can choose to stop being a part at any time. Nothing will happen to you if you decide to stop being in the study.

In addition, we may ask you to leave the study without your consent if:

- o You can not or will not follow the study directions, such as smoking only your cigarettes, collecting your cigarette butts, and keeping your laboratory appointments
- o The sponsors of the study decide to cancel the study before your last visit.

## 9. VOLUNTARY PARTICIPATION

It is your choice to be in this study or not. If you wish to be in the study you should sign this form on the last page. If you join this study you may drop out at any time and nothing will happen to you. By signing this form you are not giving up any of your legal rights.

## 10. AVAILABLE SOURCES OF INFORMATION

Any further questions you have about this study will be answered by the Principal Investigator:

Name: Dr Ann McNeill

Phone Number: XXXXXXXXXXXX

Any questions you may have about your rights as a research subject will be answered by:

Name: CERES (Consumer for Ethics in Research)

Contact: [www.ceres.org.uk](http://www.ceres.org.uk)

In case of a research-related emergency, call:

Day Emergency Number: XXXXXXXXXXXX

Night Emergency Number: XXXXXXXXXXXX

## 11. AUTHORIZATION

I have read this consent form and been given a chance to ask questions. I agree to be in this research study. I will receive a copy of this form. I choose to take part. I have been told that by agreeing to be in this study I do not give up any legal rights.

Participant Name:	Participant Signature:	Date:
Principal Investigator Signature:		Date:
Signature of Person Obtaining Consent:		Date:



**Appendix V.III Questionnaire – Visit 1 and 2**

TSNA Questionnaire- Visit 1	
	I'm going to ask you some questions about your smoking behaviour- you might recognize a couple of these from our first phone conversation.
Smoke.day	<p><b>Note:</b> Insert answers from telephone questionnaire.</p> <p>Do you smoke every day? _____</p> <p>➤ <b>If Yes, continue</b></p>
Cigs.numb	<p>How many cigarettes do you usually smoke <u>per day</u> ? _____</p> <p>➤ <b>If 10 or more, continue</b></p>
Brand.usua	<p>What brand of cigarettes do you usually smoke? *Name, strength, size, flavour</p> <p>(circle one)</p> <p>1. Marlboro Gold KS _____ Size</p> <p>2. Silk Cut Purple _____ Size</p> <p>3. Benson &amp; Hedges KS Gold _____ Size</p> <p>4. Lamber &amp; Butler KS (silver) _____ Size</p> <p>5. Other: _____</p> <p><b>*Note: Research Assistant to confirm with pack</b></p>
brand.alwy	<p>Have you <u>always</u> smoked [current brand]? (Please circle)</p> <p>YES / NO</p> <p><b>Note: If YES Skip to “Age.start”</b></p>
Brand.lengt	<p>How long have you been smoking this brand?</p> <p>_____ months _____ years</p> <p>➤ <b>If 3 months or more, continue</b></p>

Brand.old	<p><b>If NO to above:</b></p> <p>a. What brand did you smoke before [current brand]?</p> <p>_____</p>
Brand.why	<p>b. Why did you switch brands? (READ-Circle answer for each)</p> <p>i. Price                      YES / NO</p> <p>ii. Taste                      YES / NO</p> <p>iii. Health Concerns      YES / NO</p> <p>iv. Other?</p> <p>_____</p>
Age.start	<p>At what age did you start smoking daily?</p> <p>_____</p>
Cigs.max	<p>What is the largest number of cigarettes you would smoke in a day (without it being very unusual)?</p> <p>_____</p>
Cigs.min	<p>What is the smallest number of cigarettes you would smoke in a day (without it being very unusual)?</p> <p>_____</p>
Cigs.yest	<p>How many cigarettes did you smoke yesterday?</p> <p>_____</p>
Waking.tim	<p>How long after waking do you usually smoke your first cigarette of the day?</p> <p>_____ Minutes</p> <p>_____ Hours</p>

Quit.5yrs	Have you quit smoking at all in the last five years? (Please circle)
Quit.date	YES / NO
Quit.length	If yes: When did your last quit attempt end? _____ Months OR _____ Years How long did you stop smoking? _____ Days OR _____ Months OR _____ Years
Inhale.strg	Which of the following best describes how strongly you usually inhale when you smoke? (READ-Circle one) A. You don't inhale into your chest at all. B. You inhale only a little into your chest C. You inhale deeply into your chest D. You inhale into your chest as deeply as possible
Burn.time	On average, how long do you let the cigarette burn in between puffs? _____ Seconds
Puff.numbr	Which of the following statements best describes how many puffs you usually take when you smoke a cigarette? (READ-Circle one) A. You only take a few puffs on each cigarette B. You take more than a few puffs but not as many as you could C. You take as many puffs as you can on each cigarette
Puff.scale	Thinking about how many puffs you take and how strongly you inhale, overall, how "hard" do you usually smoke each cigarette? 0-----1-----2-----3-----4-----5-----6-----7-----8-----9-----10 Not at all      A little      Somewhat      Very      As hard as possible
Cig.last	How long has it been since you last smoked a cigarette? _____ Minutes OR _____ Hours
Cig.number	In total, how many cigarettes have you smoked since waking today? _____

Quit.plan  Quit.date	<p>Are you planning to quit smoking: <b>READ</b></p> <p>01 – Within the next month?</p> <p>02 – Within the next 6 months?</p> <p>03 – Sometime in the future, beyond 6 months,</p> <p>04 – Or are you not planning to quit</p> <p><b>If yes:</b> Have you set a firm date?</p> <p>01 – Yes</p> <p>02 – No</p>
Tobac.oth er  Timeuseot hertobac	<p>In the past 3 months, have you used any other tobacco products besides cigarettes, such as smokeless, cigars, pipe, bidis or kreteks, cigarettes other than study recognized, nicotine patch or gum or any other NRT products?"</p> <p>Product: _____</p> <p>➤ <b>If yes, when was the last time you used it.</b></p> <p>_____</p>
Height	<p>Finally, the last two questions will help us to understand the laboratory findings:</p> <p>How tall are you?</p> <p>_____ feet                      or _____ centimetres</p> <p>_____ inches</p>
Weight	<p>How much do you weigh?</p> <p>_____ pounds      or      _____ kilograms</p>

TSNA Questionnaire- Visit 2	
Butt.prob2	<p>I'd like to ask a few questions about the cigarette butts you collected</p> <p>Did you have any problems or general comments about collecting the butts?</p>
Butt.miss2	<p>Some people have found that its difficult to collect every butt they smoke- were there any butts that you weren't able to collect?</p> <p>If yes: Use case and try and determine a rough time and order in sequence. Record below.</p>
Smoke.norm2	<p>We'd like to get a sense of whether your smoking behaviour since your last visit was fairly typical of a normal day of smoking. Did anything unusual or different occur that changed the number of cigarettes you smoked or your smoking behaviour?</p> <p>If yes, describe</p>
Cigs.yest2	<p>To confirm, in total, how many cigarettes did you smoke since SINCE YESTERDAY'S VISIT?</p> <p>_____</p> <p><b>RA Note:</b> Make sure total matches up with collected butts + number of missing, If they don't try to reconcile which is correct.</p>
Brand2	<p>What brand of cigarettes did you smoke since last visit?</p> <p>_____</p> <p><b>*Note:</b> Research Assistant to confirm with pack</p>

brand.othr2	<p>Did you smoke cigarettes from any other brand?</p> <p>YES / NO</p> <p><b>IF yes:</b> What brand:</p> <p>How many cigarettes?</p> <p>What times of the day? [If possible, mark butt collection containers]</p>
Waking.tim2	<p>How long after waking did you smoke your first cigarette TODAY?</p> <p>_____ Minutes</p> <p>_____ Hours</p>
Inhale.strg2	<p><b>For the next few questions, I'd like you to think about the cigarettes you smoked SINCE YESTERDAY'S VISIT.</b></p> <p>Which of the following best describes how strongly you usually inhaled when you smoke? (READ-Circle one)</p> <p>A. You didn't inhale into your chest at all.</p> <p>B. You inhaled only a little into your chest</p> <p>C. You inhaled deeply into your chest</p> <p>D. You inhaled into your chest as deeply as possible</p>
Burn.time2	<p>On average, how long did you let the cigarette burn in between puffs SINCE YESTERDAY'S VISIT?</p> <p>_____ Seconds</p>
Puff.numbr2	<p>Which of the following statements best describes how many puffs you usually took when smoking? (READ-Circle one)</p> <p>A. You only took a few puffs on each cigarette</p> <p>B. You took more than a few puffs but not as many as you could</p> <p>C. You took as many puffs as you can on each cigarette</p>
Puff.scale2	<p>Thinking about how many puffs you took and how strongly you inhaled, overall, how "hard" did you usually smoke each cigarette SINCE YESTERDAY'S VISIT?</p> <p>0-----1-----2-----3-----4-----5-----6-----7-----8-----9-----10</p> <p>Not at all      A little      Somewhat      Very      As hard as possible</p>
Cig.last2	<p>How long has it been since you LAST smoked a cigarette?</p> <p>_____ Minutes OR _____ Hours</p>



















## Chapter VI

### Appendix VI.I Participant Information Sheet

Enfield   
Primary Care Trust



Haringey   
Teaching Primary Care NHS Trust

#### Smokers' and Ex smokers' views on smoking, quitting and quit smoking services

Dear Madam/Sir,

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES) publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. Please ask us for a copy, or if you wish, a copy may be obtained from CERES, PO Box 1365, London N16 0BW.

Thank you for reading this.

#### What is the purpose of the study?

The aim of the study is to find out about smoker's and ex-smokers' views on smoking in general and their thoughts on quitting and quit smoking services in particular.

#### Why have I been chosen?

We are asking all smokers and ex-smokers, who recently attended the Enfield and Haringey Quit Smoking Service for their thoughts and experiences relating to smoking and giving up. We will also recruit participants into this study, who have never attempted to quit smoking.

#### Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

#### What will happen to me if I take part?

If you decide to take part in this study (please see the section *What do I have to do?* for more information), you can choose whether you prefer our researcher to come to your home or arrange to see you at University College London or the Quit Smoking Service premises. For this study, we will ask you to fill in one single questionnaire, which contains questions about your background and assesses your past and current smoking. This should take no longer than 10 minutes to fill in.

After you have completed the questionnaire, we will ask you a number of questions about your thoughts and feelings regarding smoking; what you think about quitting and the current smoking cessation services. This interview should last around 45 minutes. We will ask you to give your consent to us tape-recording the interview so that we can analyse your comments and opinions in more detail after the interview is finished. *Any information you provide, however, is kept strictly confidential.*

#### What do I have to do?

If you would like to take part in this study, you can either contact us directly (see *Contact for Further Information* at the end of this leaflet) or you can return the *Registration of Interest* slip in the provided Freepost envelope.

#### What are the possible disadvantages and risks of taking part?

There are no known risks or possible disadvantages from participating in this study. However, a trained psychologist will be on hand to discuss any issues with you should these arise in the unlikely event of you becoming upset during the interview.

#### SPECIALIST QUIT SMOKING SERVICE

Haringey PCT, Block A1, St Ann's Hospital, St Ann's Road, Tottenham, London, N15 3TH

11/03/2005

FREEPHONE 0800 055 6255



What are the possible benefits of taking part?

By participating in this study, you may help us improve the information and support services provided for smokers and help the development of new methods to motivate smokers to quit smoking.

Who is organising and funding the research?

The study is funded by the Medical Research Council and is organised at the Health Behaviour Unit at UCL.

What if something goes wrong?

As this study does not involve any invasive procedures this is highly unlikely. However, if you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you.

Will my taking part in this study be kept confidential?

All information, which is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the Quit Smoking Services will have your name, address and any other identifying data removed so that you cannot be recognised from it. All personal information collected and used for this research will be handled according to the guidelines set out in the Data Protection Act 1998. All personal data will be anonymised to ensure and protect your confidentiality. At the initial stage of obtaining consent, you will be allocated with a number and all personal information and responses will be coded against this number.

Your personal data will be destroyed at the end of the study period (31/10/2005). Only anonymised data will be kept and stored for 5 years in a secure filing cabinet in the Health Behaviour Unit at UCL. Any analysis of data will take place in the department. Access to any personal data during the course of this research project will be restricted to the named researchers in this study.

What will happen to the results of the research study?

The findings of this study will be written up (put into a scientific report) and are likely to be available early in 2006. We will provide you with a summary of these results. We also hope to present the findings and to publish the results of this study in the near future. However, you can rest assured that you will not be identified in any report or publication.

Who has reviewed the study?

This study has been reviewed by the Barnet, Enfield and Haringey Research Ethics Committee.

Contact for Further Information

Mr Lion Shahab  
Health Behaviour Unit  
Department of Epidemiology, UCL  
2-16 Torrington Place, London WC1E 6BT

Research Team

Lion Shahab, Ainsley Hardy (Enfield & Haringey Quit Smoking Service), Professor R West (UCL)

**Thank you very much for reading this information sheet. If you would like to participate please contact (see above) or return the Registration of interest slip. We very much appreciate you help with this study.**

*Please keep this information sheet for future reference.*

**SPECIALIST QUIT SMOKING SERVICE**

Haringey PCT, Block A1, St Ann's Hospital, St Ann's Road, Tottenham, London, N15 3TH

11/03/2005

FREEPHONE 0800 057 0255



## Appendix VI.II Study consent forms



Participant Identification Number:

### CONSENT FORM

Before Interview

#### Investigating attitudes towards smoking cessation and smoking cessation services: a qualitative study.

Name of Researcher: Lion Shahab

#### Please tick box

1. I confirm that I have read and understand the information sheet dated...11/03/2005.....  
(version N . 1) for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time,  
without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of any parts of my notes at the Enfield and Haringey NHS Quit  
Smoking Service may be looked at by the researchers, where it is relevant to my taking part  
in this study. I give permission for these individuals to have access to my records. I under-  
stand that my personal data will be kept secure and destroyed at the end of the study period. ☐
4. I give consent for my interview conversation with the researcher to be audio taped. ☐
5. I agree to take part in the above study. ☐

Thank you very much for taking part in this study.

\_\_\_\_\_  
Name of Participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of Person taking consent  
(if different from researcher)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Researcher

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

1 for participant; 1 for researcher; 1 to be kept with clinic notes

SPECIALIST QUIT SMOKING SERVICE  
Haringey PCT, Block A1, St Ann's Hospital, St Ann's Road, Tottenham, London, N15 3TH  
FREEPHONE 0800 055 6255



Participant Identification Number:

## CONSENT FORM

After Interview

### Investigating attitudes towards smoking cessation and smoking cessation services: a qualitative study.

Name of Researcher: Lion Shahab

#### Please tick box

1. I give consent for my interview conversation with the researcher to be analysed. ☐
2. I understand that part of my interview conversation for this research may be reproduced in an article for publication, for a presentation at a conference or made publicly available in some other form. I give consent for interview conversation to be quoted in such work as long as it is appropriately anonymised. ☐

Thank you very much for taking part in this study.

_____ Name of Participant	_____ Date	_____ Signature
_____ Name of Person taking consent (if different from researcher)	_____ Date	_____ Signature
_____ Researcher	_____ Date	_____ Signature

1 for participant; 1 for researcher; 1 to be kept with clinic notes

SPECIALIST QUIT SMOKING SERVICE  
Haringey PCT, Block A1, St Ann's Hospital, St Ann's Road, Tottenham, London, N15 3TH  
FREEPHONE 0800 085 6275

## Appendix VI.III Ethical/Research Governance approval letter

Version 2, October 2004



**Barnet, Enfield & Haringey Local Research Ethics Committee**  
Hubbrook House  
Cookhellers Road  
Barnet  
Tel: 0208 272 5599  
Fax: 020 8372 5591  
e-mail: alison.shahab@enfield.nhs.uk

14 April 2005

Mr Lion Shahab  
PhD Student  
University College London  
Health Behaviour Unit,  
Department of Epidemiology and Public Health,  
Brook House, 2-16 Torrington Place, London  
WC1E 6BT

Dear Mr Shahab

**Full title of study:** *Investigating attitudes towards smoking cessation and smoking cessation services: a qualitative study of current and former smokers.*

**REC reference number:** 05/Q0509/28

**Protocol number:**

Thank you for your letter of 6<sup>th</sup> April 2005, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

**Conditions of approval**

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

Document Type:	Version:	Dated:	Date Received:
Application	1	11/03/2005	15/03/2005

Version 2, October 2004

Investigator CV		11/03/2005	15/03/2005
Protocol		11/03/2005	15/03/2005
Covering Letter		11/03/2005	15/03/2005
Covering Letter	2	08/04/2005	14/04/2005
Letter from Sponsor		09/03/2005	15/03/2005
Interview Schedules/Topic Guides	1(ex-smokers)	11/03/2005	15/03/2005
Copy of Questionnaire	1 - smokers	11/03/2005	15/03/2005
Letters of Invitation to Participants		11/03/2005	15/03/2005
Participant Information Sheet	2	08/04/2005	14/04/2005
Participant Information Sheet	1	11/03/2005	15/03/2005
Participant Consent Form	1 (before interview)		15/03/2005
Response to Request for Further Information		14/04/2005	14/04/2005
Consent form (after interview)	1	11/03/2005	15/03/2005
Registration of Interest slip	1	11/03/2005	15/03/2005
CV - Robert West		10/03/2005	15/03/2005
Other questionnaire (ex-smokers)	1	11/03/2005	15/03/2005
Letter from Dr. O. Avenagh, UCL Biomedicine R&D Unit		08/03/2005	15/03/2005
Interview schedule quit attempt smokers	1	11/03/2005	15/03/2005
Interview schedule no quit attempt smokers	1	11/03/2005	15/03/2005

**Management approval**

The study should not commence at any NHS site until the local Principal Investigator has obtained final management approval from the R&D Department for the relevant NHS care organisation.

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

05/Q0509/28 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely,



**North Central London Research Consortium**

Angela Williams  
Research & Development Unit  
3<sup>rd</sup> Floor West Wing  
St Pancras Hospital  
London  
NW1 0PE

E-mail: Angela.Williams@camdenpct.nhs.uk

Lion Shahab  
Health Behaviour Unit  
Department of Epidemiology and Public Health  
Brook House  
2-16 Torrington Place  
London  
WC1E 6BT

Dear Shahab,

LREC Ref: 05/Q0509/28

Title: *Investigating Attitudes towards Smoking Cessation and Smoking Cessation Services: a qualitative study of Current and Former Smokers.*

I am pleased to note that the Local Research Ethics Committee has informed us that there are no ethical reasons why your study should not proceed.

Projects are registered with the North Central London Research Consortium if they utilise patients, staff, records, facilities or other resources of Camden Primary Care Trust, Islington Primary Care Trust, The Camden & Islington Mental Health and Social Care Trust, Barnet Primary Care Trust, Enfield Primary Care Trust or Haringey Teaching Primary Care Trust.

The Haringey Teaching PCT Trust therefore grants conditional approval to begin research based on the proposal reviewed by the ethics committee and subject to any conditions set out in their letter of 14 April 2005 (received by the R & D office on 20 April). Should you fail to adhere to these conditions or deviate from the protocol reviewed by the ethics committee, then this approval would become void. The approval is also subject to your consent for information to be extracted from your project registration form for inclusion in NHS project registration/management databases and, where appropriate, the National Research Register and the UCL Clinical Research Network register.



Permission to conduct research is also conditional on the research being conducted in accordance with the Department of Health Research Governance Framework for Health and Social Care:

- Appendix A to this letter outlines responsibilities of principal investigators;
- Appendix B details the research governance responsibilities for other researchers. It also outlines the duties of all researchers under the Health and Safety at Work Act 1974. Principal investigators should disseminate the contents of Appendix B to all those in their research teams.

Further information on the research governance framework for health and social care can be found on the DH web pages at <http://www.doh.gov.uk/research/> and [www.norlar.nhs.uk](http://www.norlar.nhs.uk). Staff working within trusts covered by the research consortium can also find the information on the Trust Intranet.

Researchers are also reminded that personally identifiable information on living persons must be collected, stored, processed and disclosed in accordance with the Data Protection Act 1998. Such data may be in the form of electronic files, paper files, voice recordings or photographs/scans/X-rays. Further information on the Data Protection Act is available from your organisations Data Protection Officer or from the Consortium R&D Unit. The Medical Research Council also publishes the guidance booklet 'Personal Information in Medical Research' which is available from <http://www.mrc.ac.uk/pdf-pimr.pdf>

Except in the case of commercially funded research projects, the following acknowledgement and disclaimer MUST appear on all publications arising from your work.

*"This work was undertaken with the support of [\*\*\*Insert Trust\*\*\*] Trust, who received [\*\*\*insert "funding" or a "proportion of funding" \*\*\*] from the NHS Executive; the views expressed in this publication are those of the authors and not necessarily those of the NHS Executive".*

*\* "a proportion of funding" where the research is also supported by an external funding body;  
"funding" where no external funding has been obtained.*

This is a requirement of the contract between the Trust and the NHS Executive in which the Trust receives funding to cover the infrastructure costs associated with performing non-commercial research.

Please make all members of the research team aware of the contents of this approval. I wish you every success with your research

Yours sincerely,

Mrs Angela Williams  
Co-Acting Director of Research Operations



## Appendix VI.IV Topic guides

### OBJECTIVE

- To explore smokers' views on smoking, their thoughts on quit-attempts and quit-smoking services
- To gain feedback about a novel smoking novel intervention

- Remain neutral
- Reassure ("This is very helpful", "I understand")
- Be attentive (don't think of the next Q already)
- Note issues to return to
- Probe each Q until fully answered (don't assume you know what is said, use: 'This may sound like a silly Q but...')
- Allow time to think/reply
- Don't put words in mouth
- Open Qs
- No own personal details
- No comments re answers
- Beware of summarising ("Am I right in thinking that... or have I got it wrong?")
- Ask to save Qs for you until end
- What are the **reasons behind statement?** Ask to explain terms like 'unhealthy', 'genetic', 'bad for you', 'habit', 'addiction'
- Explore statements with **strong language** further
- If double question posed, acknowledge it
- **Rephrase** Qs to explore important issues further

### 1. Beginning the interview

- Introduction of researcher; topics to be covered/structure of interview; confidentiality; timing; confirming consent for tape-recording

#### 1.1 Background

- Name Lion Shahab, researching health behaviours at UCL
- Looking at smoking and how we can help people to stop smoking
- Interested in finding out about people's experiences with regards to quitting smoking

#### 1.2 Interview Outline

- Understand you've never seriously attempted to quit smoking?
- If that's ok, I will ask you a couple of questions about your views on smoking in general, and why you've never quit and what you think about stopping
- Also be interested to hear what you think about the current smoking cessation services, what's good and what's bad about them and how you think they could be improved
- At the end will describe a new method we are developing at UCL to motivate smokers to quit and I would very much appreciate to hear your views on that method

#### 1.3 Interview Arrangements

- Should take no longer than 45 min, depends on you
- Ok to record interview (**consent**)
- It's all completely **anonymous/confidential** and recordings will be transcribed

## 2. During the interview (main themes to be covered)

- Exploring smokers views on smoking, quit attempts, quit smoking services:

### 2.1 Past smoking history

- Example Question: 'Can you tell me a bit about yourself and how you came to start smoking?'
- Probes:
  - For how long have you smoked?
  - What initiated smoking (because of friends/family)?
  - Do you remember the situation in which you had your first cigarette ever?
    - Do you remember what your intention was regarding smoking (to try it, to become a smoker etc.)?
    - Do you remember who else was there,
    - Do you remember where you got the cigarette from?
    - Do you remember why you started? What was your motivation (curiosity, to be sociable, to be like others etc.)?
    - How long did it take before you went on to daily smoking?
  - Aware of health effects at the time? Did you expect to stop before the damage was done?

*(Smokers without previous quit attempt)*

### 2.2 Attitude towards smoking

- Example Question: 'What do you think about your smoking/smoking in general?'
- Probes:
  - Smoking because of boredom/to socialise/to keep weight down/for pleasure/to cope?
  - Why do you think people smoke?
  - What would you miss most if you stopped smoking?
  - Are you happy / unhappy you smoke?
  - Does your attitude towards smoking change/stay the same from day to day?
  - How often, if ever, do you find yourself lighting up without even thinking about it?
  - Do you accept that smoking is bad for you/your health and your environment?
  - Do you ever think about the health consequences of smoking & if so, how often?
  - Do you think smoking is going to kill you?
  - Do you regret having started?
  - If applicable: How would you feel if your children started smoking?

### 2.3 Thoughts on quit attempts

- Example Question: 'Why do you think you have never seriously attempted to stop smoking?'
- Probes:

- Would you like to quit? How often do you think about it? (If so, why have you not attempted to quit?)
- Is there pressure on you not to quit?
- Do you feel confident in your ability to quit?
- Are you afraid that you would not be able to quit?
- What would it take for you to be absolutely confident not smoker ever again?
- Have you ever formulated a plan to quit/thought about quitting?
- How would you describe yourself now in terms of your attitude to smoking?

#### 2.4 Thoughts on quit smoking services

- Example Question: 'What do you know about current quit smoking services and what do you think about them?'
- Probes:
  - Is there enough publicity for quit smoking services? If not, how could it be improved?
  - Would you be tempted to go?
  - Do you know what happens at quit smoking services?
  - If you went, would you prefer group or individual treatment?
  - What are your thoughts on NRT/Bupropion? Have you heard of it?
  - What do you know about your chances to succeed in quitting smoking if you attended quit smoking services?
  - What would an ideal quit smoking service be for you?
  - Would you be interested in cutting down in readiness for quitting & see how it goes?

*(Smokers with previous quit attempt)*

#### 2.2 Attitude towards smoking

- Example Question: 'What do you think about your smoking / smoking in general?'
- Probes:
  - Smoking because of boredom/to socialise/to keep weight down/for pleasure/to cope?
  - Why do you think people smoke?
  - What would you miss most if you stopped smoking?
  - Are you happy / unhappy that you smoke?
  - Does your attitude towards smoking change/stay the same from day to day?
  - How often, if ever, do you find yourself lighting up without even thinking about it?
  - If you were to compare smoking cravings, what did they feel like? Similar to hunger, thirst?
  - Do you accept that smoking is bad for you/your health and your environment?
  - Do you ever think about the health consequences of smoking & if so, how often?
  - Do you think smoking is going to kill you?

- Do you regret having started?
- If applicable: How would you feel if your children started smoking?

### 2.3 Thoughts on quit attempts

- Example Question: 'Could you tell me about your quit attempt? Why do you think it failed?'
- Probes:
  - Was it easy/hard at first? Did you feel cravings or similar sensations? If yes, what happened to them?
  - Did you feel confident in your ability to quit before?
  - Would you say you attempted to stop because you really wanted to or because you felt you had to?
  - Why did you attempt to quit smoking? Was there a key moment for decision that made you think 'I really have to quit'/that triggered the quit attempt?
  - Physical or Mental health issues? Social pressure?
  - Did you formulate a plan to quit in advance?
  - Did you make or notice any other changes in your life during your quit attempt?
  - When did you lapse and why did you lapse?
  - What did you think when you lapsed?
  - Did you decide to give up on your quit plans or did you try to hang in there?
  - Would you like to quit? How often do you think about it?
  - What would it take for you to be absolutely confident not smoker ever again?
  - How would you describe yourself now in terms of your attitude to smoking?

### 2.4 Thoughts on quit smoking services

- Example Question: 'What did you think of current quit smoking services?'
- Probes:
  - Which aspects helpful/less helpful?
  - Suggestions for alteration?
  - Thoughts on group vs. individual treatment?
  - Thoughts on NRT/Bupropion?
  - More information wanted?
  - Suitably prepared for quit experience?
  - Particular issues not addressed that needed to be touched upon
  - Would you be tempted to go again?
  - Would you recommend it to a friend?
  - What would an ideal quit smoking service be for you?
  - Would you be interested in cutting down in readiness for quitting & see how it goes?



*(Ex-smokers)*

2.2 Attitude towards smoking

- Example Question: 'How did you feel about your smoking then and now?'
- Probes:
  - Smoking because of boredom/to socialise/to keep weight down/for pleasure/to cope?
  - Why do you think people smoke?
  - Does your attitude towards smoking change/stay the same from day to day?
  - Do you still get urges to smoke sometimes? (If so, what do you do?)
  - Are you happy / unhappy you have quit?
  - If you were to compare smoking cravings, what did they feel like? Similar to hunger, thirst?
  - How often, if ever, did you find yourself lighting up without even thinking about it?
  - Do you accept that smoking is bad for you/your health and your environment?
  - Did/do you think smoking is going to kill you?
  - Do you regret having started?
  - If applicable: How would you feel if your children started smoking?

2.3 Experiences of quit attempts

- Example Question: 'Could you tell me about your quit attempt? What do you think helped you succeed?'
- Probes:
  - Was it easy? Did you feel cravings or similar sensations? If yes, what happened to them?
  - Did you feel confident in your ability to quit before?
  - Would you say you stopped because you really wanted to or because you felt you had to?
  - Why did you quit smoking? Was there a key moment for decision that made you think 'I really have to quit'/that triggered the quit attempt?
  - Physical or Mental health issues? Social pressure?
  - Did you formulate a plan to quit in advance?
  - Did you make or notice any changes in your life during your quit attempt?
  - Feel like a different person now?
  - How would you describe yourself now in terms of smoking?

2.4 Thoughts on quit smoking services

- Example Question: 'What did you think of current quit smoking services?'
- Probes:
  - Which aspects helpful/less helpful?
  - Suggestions for alteration?
  - Thoughts on group vs. individual treatment?
  - Thoughts on NRT/Bupropion?

- 
- More information wanted?
  - Suitably prepared for quit experience?
  - When you said you are abstinent to the clinic were you really?
  - Particular issues not addressed that needed to be touched upon?

*(All participants)*

➤ Exploring smokers views on a novel smoking intervention:

The researcher will briefly describe an example intervention based in GP practices, which aims to provide smokers aged 45 years or above with biomarker feedback to increase their motivation to quit smoking.

2.5 Feedback about a novel smoking intervention

- Example Question: 'We are interested to know what you think about this approach, please tell me anything that comes to your mind.'
- Probes:
  - Would it have helped you?
  - Any problems with this intervention?
  - Suggestions for improvement?
  - Does it make sense to you?
  - Would it scare you off?
  - Whom do you think would this intervention help particularly?
  - What would they think if they had a normal/abnormal result?

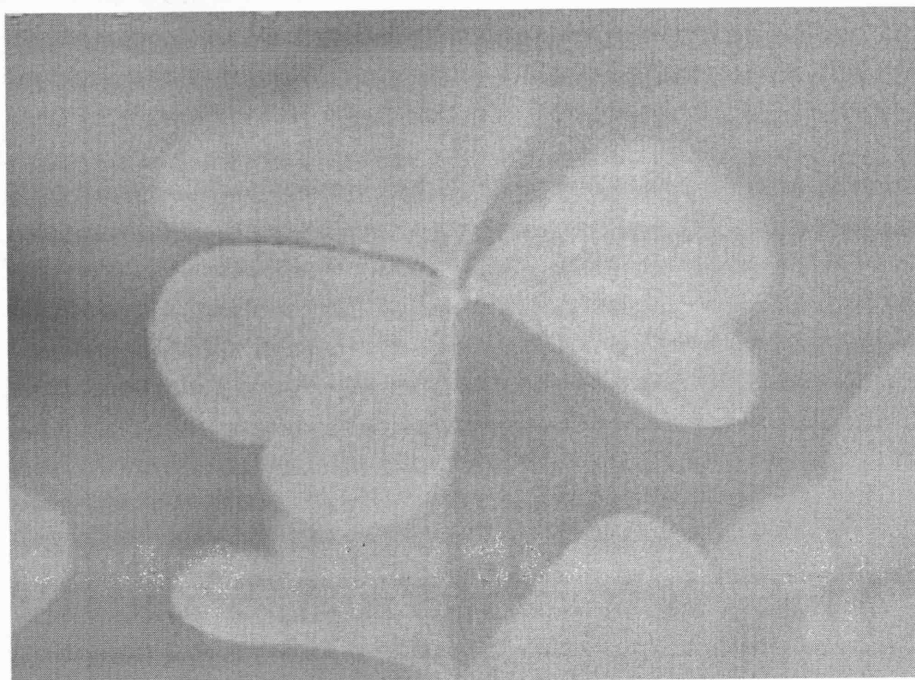
3. **Ending the interview**

- Anything else participants would like to say?
- Any important issues not raised?
- Any other questions regarding research?
- Request if they know any smokers who haven't attempted quitting who would be interested to participate in the study
- Provision of researcher contact information, should anything else come up
- Thanks

Appendix VI.V Questionnaire for ex-and current smokers

# Smoking, Quitting and Quit Smoking Services

## Smokers' and Ex-Smokers' views



Ref No:  
Group:

---

## Answering the questionnaire

For each question, please choose the answer that most applies to you.

Put a tick in the box by the statement that applies to you.  
Please tick one box only for each question.

### Example:

If you like apples you would answer the following question like this:

Do you like apples?

Yes ☒

No ☐

## PART 1: YOUR PAST SMOKING

1.) How much would you like to give up smoking/do you crave a cigarette right now?

*Please tick only one box*

- |                    |                          |
|--------------------|--------------------------|
| 1 Not at all       | <input type="checkbox"/> |
| 2 A little         | <input type="checkbox"/> |
| 3 A fair amount    | <input type="checkbox"/> |
| 4 Quite a lot      | <input type="checkbox"/> |
| 5 Very much indeed | <input type="checkbox"/> |

2.) How soon after waking do/did you smoke your first cigarette?

*Please tick only one box*

- |                        |                          |
|------------------------|--------------------------|
| 3 Within 5 minutes     | <input type="checkbox"/> |
| 2 Within 6-30 minutes  | <input type="checkbox"/> |
| 1 More than 30 minutes | <input type="checkbox"/> |

3.) How many cigarettes a day do/did you usually smoke?

4.) Do/Did you regularly get up at night in order to smoke?

*Please tick only one box*

1 Yes ☐

0 No ☐

5.) Do/did you smoke if you were so ill that you were in bed most of the day?

*Please tick only one box*

1 Yes ☐

0 No ☐

6.) Do/did you find it difficult to stop smoking in no-smoking areas?

*Please tick only one box*

1 Yes ☐

0 No ☐

7.) Which cigarette would you hate/have hated most to give up?

*Please tick only one box*

1 The first of the morning ☐

0 Other ☐

8.) Do/did you smoke more frequently in the first hours after waking than during the rest of the day?

*Please tick only one box*

1 Yes ☐

0 No ☐

9.a) If you are married or live with a partner, does your partner or spouse smoke now/did partner or spouse smoke before you quit smoking?

*Please tick only one box*

2 Not applicable ☐

1 Yes ☐

0 No ☐

b) And now?

*Please tick only one box*

2 Not applicable ☐

1 Yes ☐

0 No ☐

## PART 2: YOUR BACKGROUND

In order to be able to evaluate how representative you are of other ex-smokers, we would like to ask you a bit about your background.

1.) Age: \_\_\_\_\_

2.) Gender      1 male                      ☐  
                      2 female                      ☐

3.) Are you:

*Please tick only one box*

1 Single                                      ☐  
 2 Separated/divorced                      ☐  
 3 Married/living with partner              ☐  
 4 Other                                        ☐

5.) What is your highest education qualification?

*Please tick only one box*

1 No qualifications                              ☐  
 2 GCSE or O level                              ☐  
 3 GCE A level or similar                      ☐  
 4 Further/Higher Education or similar      ☐  
 5 Degree or similar                              ☐  
 6 Other    ☐

6.) Are you?:

*Please tick only one box*

1 In paid employment                              ☐  
 2 Unemployed                                      ☐  
 3 Looking after the home                      ☐  
 4 Retired    ☐  
 5 In full time education                      ☐  
 6 Other    ☐

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**Appendix VI.VI Transcribed interview example – Participant 22**

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L: Can you tell me a bit about yourself and how you came to start smoking?

P: I first started smoking when I was 14. I tried it a couple of times before that but I remember buying my first packet of cigarettes and being quite happy that I had my cigarettes when I was about 14. I always looked older than my age so I just had normal clothes on and went into a shop and bought cigarettes. At that time we used to smoke on the bus on the way to and from school, so there were four or five of us on the backseat of the bus smoking away on the way to school. And for cigarettes at lunch time we'd jump over the back-fence and the same on the way back. So when I first started smoking I would very rarely smoke other than at those times. So, it was getting the odd cigarette of a friend. It was when I bought my own cigarettes that I had to consciously think 'have I got enough cigarettes for tomorrow' in case I want one.

L: For how long have you smoked?

P: 12 years.

L: What initiated smoking (because of friends/family)? Do you remember the situation in which you had your first cigarette ever?

P: I was given it by a friend- it was almost like a dare. Nobody smoked at the time but she got a pack and we were 'oh we should try one and see what it's like'. That was before I properly started smoking, so I didn't like it. We were all coughing and it was not very nice; they were really horrible cigarettes as well. And then after that I started it after youth clubs or when I was out with my friends on a Friday. We'd divide ten cigarettes between two of us and smoke them. But I was never a regular smoker. It was only when I realised that I needed to be certain that I had a packet of cigarettes. This was when I was 13, before I started smoking properly.

L: Do you remember what your intention was regarding smoking (to try it, to become a smoker etc.)?

P: It was just to see what all the fuss was about. People smoked and you'd see the older pupils at school smoking and it's always what's classed as the cool gang, the naughty people at school were also those who smoked as well. And it was just to see what the fuss was about, I think. There were four or five of us and tried it. Nobody said you must try this but we all did. I am trying to think back now. I don't think it would have been a good thing, or I don't think at that age, I could have said to myself: No, I don't want to try it. Because I wanted to because all my friends were trying it and I would have felt like the odd one out. And also I didn't know the consequences of that.

L: Aware of health effects at the time?

P: You are aware that smokers are more likely to die. My nan had been a very big smoker and my dad smoked as well until about 5 or 6 years ago, but my nan had. She got other complications. But I remember going to see her and each time I went to see her she had less and less of her legs, because she got ulcerated legs and things. I know now that it is associated with smoking but I don't know if at my age then... I knew she smoked, I knew she was sick but she never at any point gave up smoking. Or never said don't smoke because this is what is going to happen. You end with no legs below the



knees. So I was kind of aware that it was bad for you and it could kill you early. But I don't think I ever really thought it could exacerbate emphysema or any of the other things that I know now.

L: How long did it take before you went on to daily smoking?

P: I think it was when I started my GCSEs, when I was 14. I think it was as people got older you could get hold of them more. And there was a summer before GCSEs when I wasn't working at the time or anything and somebody was old enough to buy cigarettes and it would just be something to do. And you'd go and have a fag. But by the time I got back to school other people had started smoking then as well, so it would be people who were your friends who you were able to get with for a cigarette. Because I don't think if it was just me and I had become addicted over the summer that I would have continued. But a few people had started, so there were other people who were smokers as well. And we all kind of looking older, so it wasn't a case of someone stealing a few cigarettes from their mum, we were able to get them yourself.

L: Did you notice the change of smoking because my friends smoke and because it looks cool to I smoke because I need to? Did you become aware of that change?

P: No. I remember being really wet and cold and making some excuse to my parents so I could go outside because I really wanted a cigarette. So it's going and get away with it and other people were smoking and just make the excuse of somebody was smoking next to me on the bus when really it had been me. I remember making that excuse of having and go and get something from the shop or whatever. So other than just wanting the cigarettes there so I knew they were there so I had them the next day, I really wanted a cigarette and going out and kind of saying I was going to see a friend or something, go to the shop and go and see a friend and then taking the cigarettes with me. I don't think I realised at the time but I kind of thought 'oh I god, I hope the weather doesn't stay bad for the rest of the week. I am going to be going out every time I want a cigarette...' And wanting to do it on my own that was... Now I think back there was a definite change there. I was kind of aware but I never really thought of myself as addicted or maybe I thought I'd get caught and I get into so much trouble that I would be made to stop by my parents but I wasn't.

L: What do you think about your smoking / smoking in general?

P: I notice it myself. Two things have made me notice it. I recently moved and I made a conscious effort not smoke in my house. So if I go to the pub or I go to somebody else's house where they are smoking I notice how much it smells. And I notice that and then it makes me think 'Oh God, I'm a smoker and I notice it what must it be like for non-smokers?'. I personally quite like them to bring in the ban on smoking everywhere. I just think it makes sense. It is also one of those things that is still classed as cool – you are kind of rebelling and you know rock stars are always pictured with a cigarette in one hand and a glass of whiskey in the other. In films as well it's all the sultry women at the bar having a cigarette. So all of the associations... you very rarely see somebody in a film who has become seriously ill because of smoking. It just doesn't make sense for the story to put in all the other things that happen in real life. So I think that there are some conflicting images that go out. I don't think that people ever check or people really care if they are selling cigarettes to somebody who's 12 or 13. You can get cigarettes very, very easily. And I never had any problem at all getting hold of cigarettes. It's odd because everybody knows how bad it is for you but people don't really stop or people

just think 'I have done it for 50 years now – doesn't matter; damage is done and I might as well enjoy it.'

L: But your view on the ban conflicts with your own smoking. How does that work?

P: I don't know. I've been to New York and Ireland quite a lot and it seemed much better. You know the environment that people are in. People do talk about it and it's true that there's a little smoking shed out the back or out of certain doors and there're heaters and stuff and a little gang of people going outside and going back in. When I have been there I have noticed I have smoked less. People I have been who have either never smoked or are ex-smokers, they feel much more comfortable. Obviously, there are also health implications for people who work in bars. But bars seem much cleaner, because they are no ashtrays to clean, no cigarette butts on the carpet. So, in my head I think it would make me smoke less, so it would save me money and eventually at some point in time I would want to give up. I know there are things that ... I know I might smoke three cigarettes in an evening and if I go to the pub and I can smoke as much as I want I smoke fifteen. And I know it's not because I need them because I know the previous evening I smoked three. But it's that whole 'I can smell somebody else having a cigarette' or alcohol as well goes hand in hand for a lot of people and I think it would just be much better. And then people would have to make that effort to think do I really want to have a cigarette? And for the people who are trying to quit I think it would just make it much better for them too. Or they would feel they could not shut themselves away and wait for a month until they have been quit a month before they can go out and see their friends again.

L: Smoking because of boredom/to socialise/to keep weight down/for pleasure/to cope?

P: I remember one thing being caught by the headmaster at school. This is when I was a bit older but ... the Isle of Man, where I grew up, is kind of a bit of an odd place, I never skived off school because there's nothing else to do. And I quite liked being at school. So I remember being caught and he was telling everybody off and pointed at me 'I'm so surprised at you I wouldn't ever have thought you would smoke. I am really disappointed.' And everybody else was lumped into the same group as trouble-makers. I was not always very bright but I was always in the top grades and doing very well, and everybody else was kind of a bit lower down. And he made a really big distinction. Maybe to me it made me still cool again. Because a lot of my friends finished at 16 and I stayed on at school to do my A-levels. And I was with a different crowd of friends, so I think then it made me distinguish myself that I am still... I might do very well but I am still a bit of a rebel or I am still a bit of a bad girl. Or it still kept that link in my head with not being this thing who did really well and got all those great grades. And then I went off to University and everybody was smoking. And I don't think I ever made a conscious decision or a conscious thought came into my head: I am addicted to these things. Like oh my god, what have I done. I just think this is really expensive. Or, yeah maybe I should not smoke regal I should smoke a different brand. I never really thought I am addicted to nicotine in those terms.

L: What do you think now then of your smoking?

P: I don't know. Especially working in the department I work in, I am the only smoker and that is unusual. Everywhere else I worked there's been somebody else, everybody tells me off. But I do like smoking and maybe it's an association thing. But if I have a really crappy day or something has happened or I have been working really hard. Just

looking forward to that – going out and having a cigarette – it's just really nice. A thing I look forward to. And if I wanted a cigarette and I finally get one, it's huge sense of 'ahh..' finally. Or you sit down at the end of the day and it's like you can take your time, have a cup of coffee or a pint and have a cigarette.

L: What else does a cigarette mean to you?

P: I suppose it means a break. I very rarely take a lunch break or anything like that. It's the time of day when I can go and... Or now that I don't smoke in my flat, it very much means when I am out and having fun as well. Because a lot of my friends now do smoke or we go to places where you can smoke. And it's very much associated with going out for dinner or going around to my friends house for the night, going to a party. So, it's very much associated with that I think.

L: Do you still associate being a rebel with having a cigarette now?

P: I don't know. Perhaps. It's a bit of a contradiction work [public health] and to smoke. And I kind of think when I used to work with a lot of nurses, and there are different reasons why they smoke, but it was kind of... nobody can ever understand why you smoke. And maybe I quite like not being normal or average, I don't want to be lumped in with the same kind of group of people. 'Oh yeah, that's the sort of person you are'. Maybe I still want kind of just not be or do what's expected.

L: Why do you think people smoke?

P: I worked with nurses and it is very much a valid or an accepted reason for them to go outside and have a proper break. But nursing is a bit of an anomaly. Some people smoke because they think it makes them part of the gang, I suppose. And nobody has ever told them it's ok not to. People think that it's a weakness, I suppose, to give up something that you are addicted to. You should just keep smoking. Also, I don't think people have kind of been given not enough support but don't realise that they can stop. It takes them a bit of time because you often hear of people quitting for three or four days and then starting up again and there's a real sense of failure. And I think that maybe other people don't understand that that's ok, you know, it's difficult. There is conflicting... not conflicting information but there's stuff that does go out to the media about if you quit smoking by this age your mortality risk decreases if you stay quit for X amount of years. And I think people, especially women, use these things as excuses. I also at the back of my mind think 'Crickey, if I met somebody and decide to start a family I would stop'. And in my head that's kind of a big enough reason that I am going to want to. And also, I think people don't believe that they can quit, that they don't believe that they have the capability or the will power, you know or all their friends smoke or their partner smokes and they just don't think that they are gonna be able to do it, so they don't try. Because they fail and they don't want to be seen as a failure so they just keep smoking. I mean there are other people who do it because it is complete rebellion. I know there is work done on young British Asians, the rates of smoking in young Bangladeshi or something? It's seen as something that's you are just not supposed to do, so people show off almost.

L: Any other reasons you can think of why other people smoke?

P: I was gonna say, if a lot of other members of their family do so they don't see it as a negative thing. Or if they started young, people wouldn't notice because everybody else

in the family smokes. But sometimes that obviously works the other way round that people really don't want to smoke if their parents smoke. I think if people have seen a family member really suffering and somebody has said that's because they smoked 40 a day for however long, then they are more aware of the risk. But only because it's so emotive to them that image of somebody being sick. And I suppose that works in the other way that they think: my parents have smoked for years and they are fine, there's nothing wrong with them. And all this information is nonsense.

L: Are you happy / unhappy that you smoke?

P: I am quite happy that I smoke. I am unhappy that I didn't stop when I was 18. My life changed as you go to University or you move away; there are times in your life when you are more in control of certain things than others and I think when I was 17 or 18, yes I was addicted but it wasn't quite as engrained in me and my social life and everything else as it is now. I think that it would have been easier for me to stop then it will be if I try and stop now after 12 years. So, I think in my head it's like 'Well, I smoke now' and I don't particularly want to give up now but I will. I don't think I would succeed now if I tried to give because in my heart of hearts I don't want to. But I think when I think back there were times when it would have been much easier to give up and I think I am unhappy I never really thought about it. If somebody had made a spreadsheet of how much money it's gonna cost me or... maybe it would have made no difference at all. Maybe if my parents had caught me and basically said 'you are not getting any money for university or any of this stuff' maybe it would have been a kick up the backside to really think about it. But I never really thought about the fact I was addicted to cigarettes and 8 years down the line still being addicted.

L: Does your attitude towards smoking change/stay the same from day to day?

P: I think it's something that's quite constant. I am always very annoyed if I am eating and someone else is smoking next to me and things like that. So I don't mind walking outside of a building and having a cigarette out there. It's fine. One thing that annoys me most is if I'm sat down with a group of people and I say 'Do you mind if I smoke' and they all say 'No, it's fine'. And you find out later on that it really, really bothered somebody. That annoys me a lot because I don't mind if someone asks me not to smoke. So that doesn't really annoy me but I think because I know that makes me smoke less.

L: How often, if ever, do you find yourself lighting up without even thinking about it?

P: No, I don't do that very often. If I am in pub with a group of friends, I kind of light up and then think I only had one half an hour ago. But I don't think I ever ...

L: So are you quite conscious about having a cigarette?

P: I don't ever remember that behaviour having one there and having another one. There's times when I have thought 'O gosh, I really don't want this but I have light it now so I might as well smoke it'. I don't know if that's more being distracted or whatever.

L: Do you accept that smoking is bad for you/your health and your environment?

P: Yeah.

L: Do you ever think about the health consequences of smoking & if so, how often?

P: I don't think about it every time I light a cigarette that it is doing this and that to my body. I think it's the area where I am working and I know a lot more about it and maybe I am more aware of what sets me off wanting a cigarette and what I think about it. But I never sit there and look at a pack of cigarettes and think this is going to do this to me. In the wider terms I probably understand better than other people what the risks and rates are and all morbidity and mortality data and things, so I am very aware of it. But I never really... I don't know, I keep thinking to myself that I am young enough to give up so it doesn't matter.

L: Do you think smoking is going to kill you?

P: I'd like to think that it wouldn't. No, I never think I am gonna die because I smoked. I am aware it's gonna make me look old, give me wrinkles. But I never think it's going to kill me in those terms.

L: Do you regret having started?

P: Yeah.

L: How would you feel if your children started smoking?

P: Oh god, I would be so disappointed. But I remember my dad talking to me and saying exactly the same thing. Saying 'it's so hard to give up once you have been smoking a long time and it really does affect your health' and telling me how much it's going to cost and your clothes will smell. And I remember just not being interested at all and not being bothered. I was 'Oh, I am 17 now'. Because I working and I was still studying but I was earning my own money so I could spend my money on what I want. But I would be so disappointed.

L: Did he tell you before you started?

P: No, it was after. It was kind of just before I was going to university so I was about 17 when they found out that I smoked.

L: Do you think that there's anything one can do to prevent young people from starting in the first place?

P: If you couldn't buy cigarettes until you are 18 and you had to buy them from a specific shop and you couldn't buy them from a specific shop or anything like that, you had to buy them over the counter so somebody had to look at you and decide how old you were. I know that people start smoking by getting them of older brothers and sisters or getting somebody to buy them. It's like people starting drinking. But that would probably have stopped from having a couple of cigarettes to be able to go and consciously buy a packet of cigarettes every three or four days. You see if my parents had told me not to, I would have said what can you do? Everyone has to smoke outside now, there's no smoking rooms in offices or anything anymore. If they bring it in the bars and restaurants, everybody's going to be huddled outside having a cigarette. That would make it not seem quite as much fun and quite as enjoyable. Because anything medical, you don't think of that. When I really was kind of smoking properly by the time I was 16 or 17, I'd say I was definitely a proper smoker, I never thought that I'd

still be smoking at 26. I always thought I'd give up and it would be fine. And I never really thought any longer than that and how much money it's gonna cost. I kind of thought well I am going off to university, so I smoke at university and I give up when I quit and I give up when I get my first job.

L: Why do you think you never seriously attempted to stop smoking?

P: I never really wanted to enough to know that I would be able to stay quit. I think I have got enough will-power and, you know, I would be able to change my behaviour and my friends would be very supportive. They wouldn't smoke near me if that's what I asked them not to do or whatever and I would get nicotine replacement and stuff. So, I know it's very strange. If I tried to quit now, I know I could probably do it but I don't want to stop. I give up alcohol for a month and not think about it but if it's giving up cigarettes I'd be like 'Oh, I don't really want to.'

L: Do you know why you don't really want to?

P: I don't know. The work thing, it's not a big thing because nobody else at work smokes, but I do feel like I'm getting a break when I go for a cigarette. But I mean there is other things. I keep saying, well not saying, but I don't smoke in my house so I know that won't be a problem when I do give up. I am not seeing anybody at the moment, but if they didn't smoke then I would be more likely to. I do smoke lower tar cigarettes now then I used to. I think I am kind of gearing myself up to eventually deciding – right, today is the day. A lot of friends of mine are saying 'I'm giving up' and then 3 weeks later they are smoking or they steal a cigarette from me. And I am like 'I can't believe you've done it'. And then I think that's a really bad thing to say, it's really negative about the fact somebody started smoking again. And I think I don't like to fail, and I think, no matter what situation I put myself into, I don't want to give up enough now. And I think I would fail, so I don't want to fail.

L: Do you think about quitting at all?

P: I do want to quit at some point. But I can't see myself trying for the next months.

L: How often do you think about it?

P: Maybe about once a week, or I am somewhere I can't smoke and I want a cigarette and I just think 'Gosh, I wasn't a smoker I wouldn't be so distracted'. I was in a really, really dull lecture yesterday afternoon, and all I could think about was 'I really need a cigarette'. And I think half of it was I didn't really want a fag, I was just bored. I just got really distracted by wanting a cigarette and I thought if I wasn't a smoker, I'd be paying attention or this lecture really is crap. And it was just that was in my head that I wanted a cigarette and I kind of thought if I wasn't a smoker this wouldn't be a problem. And then kind of looking in my purse and I've got two quid and I'm like 'I have to get some money out to go and buy some cigarettes' because you can't buy cigarettes for under £3. So, I do... financially it just makes complete and utter sense to not buy cigarettes. Yeah, so I do think about it now and again. It just annoys me sometimes that fact that I smoke.

L: Is there pressure on you not quit?

P: No. There's nobody... no, I think if I did try everybody would be very supportive.

L: Do you feel confident in your ability to quit?

P: Not at the moment. I think if I tried now I wouldn't do it, I wouldn't succeed, so I am not gonna bother trying. I do want to give up eventually; I don't think I would succeed this time so maybe I think I don't want to try.

L: Are you afraid that you won't be able to quit?

P: Yeah, I'm afraid I'd start smoking again and everybody goes 'Oh, yeah, I knew she couldn't do it.

L: But you feel that as some point in the future you would be able to quit?

P: Yeah, I also think I wouldn't tell anybody that I was quitting in case I start smoking again. I never really thought about it because I always think one day I will give up but why I don't decide today is the day I give up, I don't know.

L: Is there something that would make you absolutely confident that you would not smoke ever again?

P: Not sure. I think if all of my friends quit and I was the only one, then it would make me think 1.) that I could do it if they could all do and 2.) there wouldn't be the temptation there any more. That would kind of make me really think, I've got to. If everybody else can and they have been smoking longer than me or they smoke more than I do or their partner smokes, it would make me really think 'Yeah, I can'. Or if met somebody and they really, really hated the fact that I smoked.

L: Did you ever formulate a plan to quit?

P: No. The only thing I did do is I don't smoke in my flat that I just moved in to.

L: How did this come about?

P: It was newly decorated and I thought I don't want this place to smell. I don't want this flat, people to walk in here, and think a smoker lives here. And you do walk into places and they do smell of smoke and there is ashtrays and I just didn't want that to be what my flat was like, so I made the decision that I wasn't going to smoke in it.

L: How would you describe yourself now in terms of your attitude to smoking?

P: From a public health point of view smoking is very bad for you. I do think personally the government is pussy-footing around and need to kind of sort things out. I know there's always the argument that the taxation that they get is.... That's why they don't want too many people to give up smoking.... I know I enjoy smoking, I know I like it. I know I don't want to give up yet but I know it's bad for me but I know that... Yeah, it's odd to think about it. See, it's other things... I really don't like walking down the street having a cigarette. I don't do that.

L: Why?

P: I think it looks really common. I kind of stand outside the building or I'll do it in a place I can. There are negative associations with smoking and I would like to think I wasn't that kind of person and maybe it's a bit of the rebellion thing. There's the scientist coming in now and I go and get myself a glass of red wine and have a cigarette and chat to people 'Oh' bit surprised by my behaviour.

L: What did you know and think of current quit smoking services?

P: I know if you go to your GP you can ask for Zyban to help you give up but I don't quite know under what circumstances you can get that or not get that or if you can get other NRT. I know that they are two separate things but I know that you can get Zyban from your GP but I don't know about NRT. I do know they are stop smoking clinics, which you are referred to by your GP? I am not sure. They are kind of advertised here and there but I never pay enough attention to it.

L: Do you think there's enough advertisement?

P: Things that I notice are the one's that say: You must stop smoking as opposed to stopping smoking is really difficult and this will help. It's always: smoking is bad for you and that probably has an effect for certain people in the population but for people who already smoke – I see one of them and I switch because I know it's going to show me blood and guts. But it's very really kind of an encouragement. You do get: speak to your GP about giving up smoking and they got the adverts on the bottom of cigarette packets with a free phone number I think now as well. About your pharmacist and GP about giving up smoking but as to what you can get via the NHS I don't know.

L: Would you be tempted to go to one of the services?

P: I think so. I would really be worried though that I would be like the only girl under thirty who's trying to quit. Yeah, it would depend. There are a whole lot of logistic things but if I really wanted to give up, I would you know make the time and effort. But you get the impression it's gonna be a bit like AA. 'I have been smoking for 12 years. It's my first time to try and give up.' And it's just like... that's the impression I have of them and I kind of think what on earth good use is that for me at all. Do I really want to hear about Dave who is 55, who is giving up smoking as well. I don't know what's involved in stop smoking clinics.

L: Thoughts on group vs. individual treatment?

P: Oh, I didn't know that. Um, I don't know actually. Individual would be fine only if I knew the person who was helping me is an ex-smoker. I kind of... anything anybody does, if they have never been through it themselves, then I would just that they were preaching at me. So obviously, a group situation helps that when everyone is there and, you know, chatting about everything together. And the problems they've had and the things that would set them off wanting a cigarette. But I know what the group sessions would be, how involved they would be or what you talk about and what you discuss. Whereas I think on an individual level, you feel much more like in control what this hour of your time is going to be. In a group situation you get the impression you might be sat there for 50 minutes bored out of your brains.

L: Thoughts on NRT/Bupropion?



P: Zyban, I don't actually know what it does. It stops the actual addiction? I never really... I always thought to myself 'If I went on NRT would I just get addicted to them?' Addicted to the patches? or feel like 'Oh, my god, I haven't got a patch with me today.' That whole kind of 'Oh my god, I haven't got a packet of cigarettes and there isn't a shop for 15 miles'. Would I get that with NRT? But I don't think... because there are days if I am busy or I am doing something else, I might not have a cigarette until 6 pm in the evening. Whereas at work, if haven't had a cigarette by 10 am or on my way into work, I am like I really have to have a cigarette. But you know, so I don't know how good the nicotine replacement would be. And I don't know how well one works in comparison to the other. Or does it depend on the person? I would be really weary of taking something that would interfere with my brain chemicals. Or start messing around with that kind of stuff.

L: What do you know about your chances of quitting success if you attend the services?

P: I didn't know that [before the talk at the weekend]. I kind of always assumed people lie as well and if they go to these things that they are not honest and that maybe the stats themselves are a bit skewed. I don't know.

L: What would an ideal quit smoking service be for you?

P: It would be something that I could go to whenever I wanted to? So more of a kind of open door kind of maybe a regular once a week thing or... I don't know how often they recommend you do it if you want to give up. But something that I could go to when I really felt like I was gonna have a cigarette and I could just go and complain to somebody. And just get it off my chest and then kind of, you know maybe just get a bit more of a handle on it. I think if I gave up I would just have a dreadful day or something would happen and I'd just go 'Sod this, I am gonna go and have a fag' and just think 'Sod, I am giving it all up, whatever'. The situation where I could get in touch or call somebody and say 'Look, you know, just put my feet back on the ground and tell me I don't need for whatever reason'. I think this maybe would appeal to me because I don't think it's the giving up - it's not having enough willpower not to give in. So, I think would be pretty confident I could stop and not smoke for 3,4, 5 days but for me the problem would be that one trigger. And would I just go: 'That's it, I am gonna smoke' or blaming having a bad day or being stressed out on the fact that I am giving up. I need something to keep me realistic about what was going on.

L: So, would somebody who'd tell you if you see a trigger do this...

P: Perhaps, or tell me that I am not being completely over-reacting or being a bit stupid that yeah, it will pass or go and do this or people have suggested going brushing your teeth will make you stop wanting to have cigarette or going and doing this. Or, you know, just sod it and go and buy a big bar or chocolate or whatever or something to kind of... instead of me in my own head trying to calm myself down or trying to decide that I don't want a cigarette... you know that kind of thing would appeal to me.

L: Would you be interested in cutting down in readiness for quitting & see how it goes?

P: Well, I try to... yeah, I think because I don't smoke where I live now I feel like I have made a big change. But for me, it's the day... well, not necessarily the days, but you know if I am out with my friends and stuff I just think 'Oh tonight, I am out for dinner, few glasses of wine I am gonna smoke'. And I probably still do that even if I cut

down during the week, you know. But I don't think cutting down wouldn't make it that much easier for me to stop. Because I managed to cut and cut down that's not been a big problem, so I think maybe giving up is gonna be really difficult no matter how hard I... cutting down seems really easy. I think I am just waiting for it [smoking] to become really difficult.

## DESCRIPTION OF INTERVENTION

L: Would it help you if you still smoke at that age?

P: Um, I don't know. I always feel like I should know better because I do have all of this knowledge about what it does to your body and everything. So if I was still smoking then, I would be pretty determined to keep going. But actually, really properly seeing me and how bad it was and knowing, you know, what it was doing and like you say, if you only have two carotid arteries and you mess up one or bother that's it, you are a goner. So, it might just be a real eye-opener. But, I don't know, I'd like to think I wasn't smoking at 45.

L: Whom do you think would this intervention help particularly?

P: To me, it screams out it would be the lower SES who really didn't take on board or conceptualise that those disease risks are yours. The people who have had symptoms or asthma and stuff like that and someone says: Look this is what is happening to you, it's not just chance or fate or bad luck or whatever, it is because this is what you are doing to your body. Um, you couldn't do it with anybody younger, because they would just not think it was gonna happen to them. Or people who, maybe people who have never tried to quit it may have more have an effect on, because if everything else hasn't worked it's almost like your last chance to get them to quit.

L: Any problems with this intervention?

P: The whole logistics of it, getting people in, getting them and then why smokers get it and non-smokers don't. I mean ok, I might know that there's nothing that a doctor can do or tell me. Say, I never smoked and I did have plaque, there's probably nothing they can do and people would be like 'Oh my gosh, all these smokers have all these medical checks, all of that money being spend on them to make them stop smoking'. There would be that kind of reaction, I think, from most other people. Obviously, you would have to provide correct information for people to say, you know you couldn't just give them a picture and say: That's yours and that's a healthy one. There would have to be a process of discussion beforehand and afterwards and what was then going on in the rest of your body, so that people could answer if they have never really considered what's going on in their own body, there'd need to be somebody there who could do that and the people who were interested and who were shocked could then generate more interest in giving up and what it's doing.

L: Suggestions for improvement? What would they think if they had a normal/abnormal result?

P: I never thought of that. They probably continue. If they thought that they weren't any sicker than a normal person. I found out ages ago, and again it's the weekend, because if you give up before you are 35 your disease risk decreases to that of somebody who has never smoked. And that sticks in your mind. You think that you can get away with

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smoking and you worry about it in 4 years time or you give up if you hit a certain age or if your partner has children or you know whatever you come to. It could work in the opposite way that people would think that they could get away with it. They'd go back and expecting another one and say: Have they got any worse doc? And if they had, I'll give up, I promise.

L: Anyway to get around this kind of problem?

P: Don't know how you get ethically around it. Just not show them, just say it's part of the routine, not actually show them the picture. Just say, oh yeah your arteries are worse, and people who do have really bad arteries actually show them.

L: Would it scare you off?

P: Yeah, because it would be the first thing that I can think of that somebody is actually physically able to show me that, you know, what is going wrong, and it's something that would kill me. Somebody could tell me that I look older than my years or that my clothes smell or that I am really skint all the time but all of those things I know and I don't necessarily know what damage my arteries have had.

L: Any other questions/thoughts regarding research?

P: One thing that I always wish that I had stopped much earlier and I can't think of what else can be done for people who are 18, 19, 20 before it is really engrained in their working life and their habits and attitudes but I don't know what can be done there. I do think not smoking in pubs and public areas, I genuinely think that will help. And as a smoker, even if I still continue to smoke the next 5 years, I think it would be very good if it was brought in.

Appendix VI.VII Example Chart – Positive attitude towards smoking

Identifier		Positive appraisal of smoking		
		Positive view / enjoyment of smoking	Smoking to deal with stress	Smoking as friend / shield
Ppt 8	Never quitter		Thank goodness I have a cigarette, at least I sit down. It's a stress thing. {85ff}	
Ppt 18	Never quitter	I enjoy smoking. There are times when I think 'yeah I quite enjoy this'. {69ff}	I can find myself in a stressful situation and find I'm smoking quite a lot. {254ff}	
Ppt 19	Never quitter		It's a stress thing I think mainly. Certainly the amount that I've smoked in the last couple of years has been completely correlated with the hours that I was working, with the PhD that I was writing. So it is mainly stress avoidance and I try to reduce stress. {69ff}	
Ppt 20	Never quitter	I just liked it, I don't really know why. {25} But it doesn't mean that there is nothing good about smoking. {73} I don't regret starting in the first place when I was a teenager, no. {109ff}		
Ppt 21	Never quitter	I just enjoy it, I enjoy smoking. {69} I've always met loads of interesting people on smoke breaks outside work and generally lots of my friends smoke so it's been a shared experience there. {73ff} No, I don't regret [having started]. {121}		I enjoy taking five minutes away from my work up to ten times a day and having a cigarette. {69ff}
Ppt 22	Never quitter	I am quite happy that I smoke. (National Cancer Institute, 1999) I know I enjoy smoking. {153}		I suppose it means a break. {48}
Ppt 23	Never quitter	I don't really regret it. {120} I love smoking cigarettes. {152}	It kind of makes me relaxed I guess. {69} Then it was like 'I need a cigarette', there were some bad news or whatever. But it wasn't like just out of the blue 'I need a cigarette'. {49ff}	The cigarette became the time of reflection or something like that. {69}

Identifier	Positive appraisal of smoking		
	Positive view / enjoyment of smoking	Smoking to deal with stress	Smoking as friend / shield
Ppt 2	Unsuccessful quitter No. It was totally, absolutely heaven to smoke. {57}		So there's an element of loneliness, there's an element of not being fulfilled. So sometimes my cigarette fulfills me because I'm bored. {73ff}
Ppt 4	Unsuccessful quitter	I think it's more linked to stress as you get older, it's something you are hanging onto. It's like you really need it to survive. {67ff}	I suppose that's my time [when I smoke]. {63} I don't smoke as much, it's not on my mind all the time, as it is when I'm feeling quite down {99ff}.
Ppt 5	Unsuccessful quitter	I think this started because I was a single mum and I'd moved away from a lot of friends and I'd got quite a stressful job and suddenly I noticed that I was buying a pack every other day and then that was it. {57ff}	Cigarettes seem to be my only solace. {69}
Ppt 7	Unsuccessful quitter	I still enjoy it a lot. {48}	
Ppt 9	Unsuccessful quitter	I enjoyed doing it and I was drinking and partying. [...] I do that as a relaxation. {25ff}	
Ppt 12	Unsuccessful quitter		
Ppt 14	Unsuccessful quitter		[Smoking is] only thing I have that is just for being on my own and being left alone I have time to think my own thoughts [...] It's my sort of crutch really. {72ff}
Ppt 16	Unsuccessful quitter	I'm happy that I smoke. {94}	I do enjoy it because it occupies me and makes me apparently relaxed. {94ff}

Identifier	Positive appraisal of smoking		
	Positive view / enjoyment of smoking	Smoking to deal with stress	Smoking as friend / shield
Ppt 1	Successful quitter		
Ppt 3	Successful quitter Well I do and I don't. I had a great time smoking - I have to tell you that. I loved it; it gave me a lot of pleasure. I preferred to have not, but I did have a lot of fun. {137ff}		
Ppt 6	Successful quitter	So [smoking] certainly was to cope with stress. {41}	
Ppt 10	Successful quitter No [don't regret having started to smoke].{183}		It was a friend, it wasn't just smoking [...] I enjoyed sitting back by myself having a cigarette {95ff}
Ppt 11	Successful quitter		
Ppt 13	Successful quitter I liked [smoking] too much. {40}		[Quitting smoking felt] like a grieving process. That's the only way that I can describe it. {180ff}
Ppt 15	Successful quitter Yes I enjoyed [cigarettes], I used to relish everyone of them, I used to really, really enjoy it. {65ff}		
Ppt 17	Successful quitter I don't really regret it as such. {105}	It actually meant relaxation. {49}	

## Chapter VII

### Appendix VII.I Participant information sheet

#### Royal Free and University College Medical School

Department of Epidemiology and Public Health

University College London

Gower Street Campus



HEALTH BEHAVIOUR UNIT  
2-16 Torrington Place  
London WC1E 6BT

#### PARTICIPANT INFORMATION SHEET

**Title of Project: Cigarette testing protocols and human smoking behaviour study**

**Principal Investigator: Ann McNeill**

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES) publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. Please ask us for a copy, or if you wish, a copy may be obtained from CERES, PO Box 1365, London N16 0BW.

Thank you for reading this.

#### **12. PURPOSE OF THIS RESEARCH STUDY**

- a) We are asking you to be part of a research study to measure chemicals that are in cigarettes and enter your body when you smoke. We want to know how chemicals in cigarette smoke are absorbed by smokers and will answer this question by comparing the levels of chemicals in your saliva, urine and breath with the levels of chemicals in the smoke from your cigarettes. We also want to know how much you smoke so we will want you to collect all of your cigarette butts for a one day period and smoke your cigarettes during that period through a device that measures how you smoke. About 200 people will take part in the study. Everyone who takes part in this study will be smoking the cigarettes they usually smoke. We will not ask you to smoke any other type or brand.
- b) If you are a woman, and there is any chance that you may be pregnant, you cannot take part in this study.

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### 13. PROCEDURES

If you take part in this study, we will ask you to visit the laboratory in the Department of Epidemiology and Public Health at University College London on two occasions, 24 hours apart. All visits to the laboratory will be in the late afternoon/early evening and each visit will last between 30-60 minutes.

First Visit. During the first visit, you will be asked to do the following:

1. Answer a short questionnaire about your smoking history and current smoking behaviour. We will also ask to see a pack of your cigarettes so that we can verify the brand you smoke.
2. Provide a saliva sample by chewing on a small piece of cotton until it is soaked with your saliva. You will then place it into a special container. This sample will be sent to a laboratory to find out what chemicals from cigarette smoke are in your body.
3. Provide a urine sample which will also be sent to a laboratory to find out about other chemicals from cigarette smoke in your body.
4. Blow into a machine that measures the amount of carbon monoxide in your breath. You will take in a deep breath, hold it for 15 to 20 seconds, and then blow into the machine. This process is then repeated a second time to give two measures.
5. We will then explain to you how to use the smoking machine (a sterilized cigarette holder device that measures the kind of puffs you taken when you smoke). We would like you to use the device for every cigarette you smoke until the next visit. It is particularly important that you use it for the first cigarette you smoke upon waking, and that you do not allow any other smoker to use it. It is also important that you smoke only the cigarettes that you tell us you normally smoke, but you can smoke as many as you would normally would.
6. We will also explain to you how to collect your cigarette butts and give you a case which contains small tins in which to store the butts in the order you smoke them. Until your return visit, you will collect all cigarette butts into the tins, record the date and time and place where the cigarette was smoked on the tin using the pencil provided, and then place the individual tins in the case that we will give you.
7. You will then practice by smoking one of your regular cigarettes using the smoking machine and collect the first butt in the tin provided.
8. After you smoke the cigarette, you will blow into the carbon monoxide machine again to see how much carbon monoxide you have in your breath after smoking. As before, two measures will be taken.
9. You will schedule a time to return to UCL the next day.

Second Visit.

You will come back to the laboratory to drop off the smoking device and cigarette butt case. We will ask you questions about how you smoked during the time between visits,



your experience of using the smoking device and will take a saliva and urine sample, and two breath samples as in Visit 1.

#### Follow up telephone call

You will receive a follow up telephone call 6 months after your participation to assess any impact of the study. This will enable us to feedback the overall results of the study and answer any queries that you may have.

### **14. POSSIBLE RISKS OR DISCOMFORT**

c) The risks of taking part in this study are the same risks that you have every day with regular smoking. There is no risk in using the device that tests how you smoke. It is like smoking your cigarette with a cigarette holder attached. There is very minimal risk in giving saliva or urine samples. Chewing the cotton should provide no risk as long as you are careful to not swallow it. Breathing into the device to measure carbon monoxide should pose no concern. All of the methods used in this study have been used before. We will tell you of any new information developed during the study that may affect your willingness to continue in the study.

d) It may be hard for you to collect all of your cigarette butts between visits and may require you to change some habits. We will try to make this as easy as possible by giving you a small collection case that can fit into a pocket or purse for you to use if you go out in public between visits. It will be important to not throw butts away, and to not put them out by dipping them in any fluid. You should not take part in this study if you think these changes will be too hard to do.

e) Coming to the laboratory at the times you are scheduled will be very important and may be inconvenient. We will do everything we can to meet your schedule.

### **15. POSSIBLE BENEFITS**

Participation in the study is not expected to benefit you directly. As you may know, smoking causes lung cancer, heart disease, and emphysema and may complicate pregnancy. Quitting smoking now greatly reduces serious risks to your health.

We will give you your carbon monoxide levels at the end of the study. We will also give you information about smoking and smoking cessation services which you may find helpful. However, the decision to use these services is your decision and taking part in this study will not require that you consider quitting.

Other people may benefit by you taking part in this study. For instance, if the study finds that certain cigarettes cause smokers to get more dangerous chemicals in their bodies, warnings can be given to people who smoke these cigarettes or who are thinking of starting to smoke.

### **16. FINANCIAL CONSIDERATIONS**

In appreciation for your time and any inconvenience, you will receive £50 on completion of the second visit. Other than the cost of your transportation to the laboratory, no additional cost to you is expected to result from taking part.

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## **6. CONFIDENTIALITY**

Data collected and stored in this study will be done so in accordance with the Data Protection Act 1998. For your protection, we will assign you a number that will be used to label all information and all specimens. The personal information, such as your name and how to contact you, will be kept in a separate file that is locked away at University College London and is destroyed after the study is completed in approximately 2 years. The saliva sample and cigarette butts will be destroyed once analysed. No personal information such as your name or contact details will be on the specimen bottles or survey data.

Your identity in this study will be treated as confidential. The results of the study, including laboratory and other data, may be published for scientific purposes but will not give your name or include information that will identify you. However, any records or data obtained as a result of your participation may be checked by the group that oversees research to make sure that human subjects are protected.

## **7. TERMINATION OF RESEARCH STUDY**

You are free to choose whether or not to take part in this study. You can choose to stop participating at any time. In addition, your taking part in the study may be stopped by the investigator without your consent if you are unable or unwilling to follow the study protocol, such as smoking only your cigarettes, and keeping your laboratory appointments; or if the sponsor of the study decides to cancel the study before your visits are complete.

## **8. ETHICS REVIEW**

This study has been approved by University College London's Committee on the Ethics of Non-NHS Human Research.

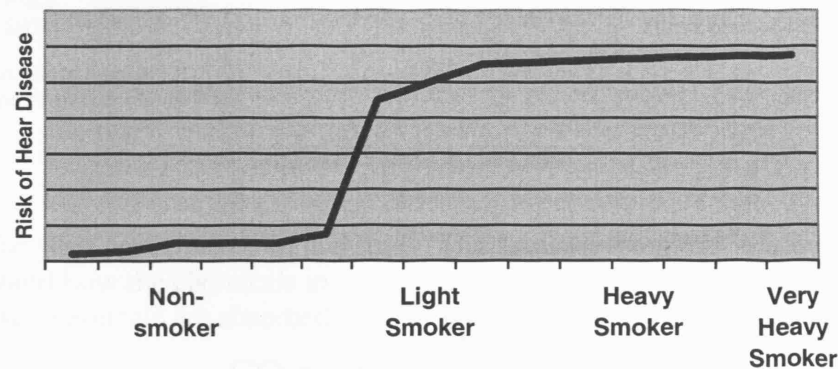
## **9. AVAILABLE SOURCES OF INFORMATION**

All participants will be given a copy of this Information Sheet and the signed consent form to keep. If you have any questions later or if you require additional information about the study and your rights as a participant please feel free to contact the Principal Investigator Dr Ann McNeill, on XXXXXXXX. Please also use this number in case of a research-related emergency.

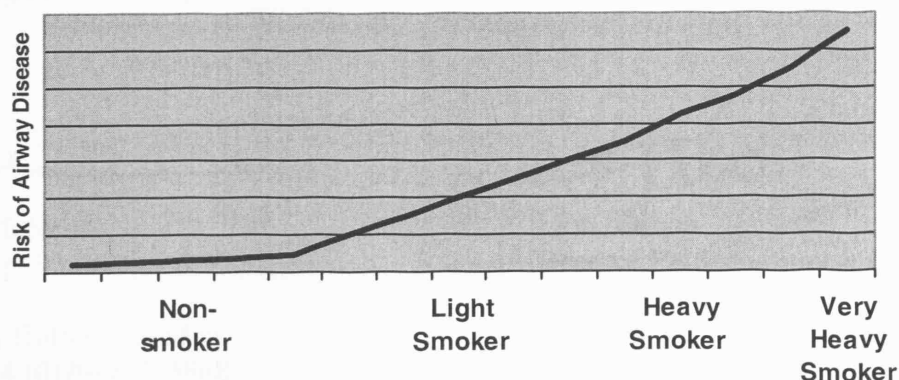
## Appendix VII.II Intervention schedule

## Intervention

- Smoking harms your health
- E.g. smoking increases your risk of heart problems
- Relationship CVD-smoking is sigmoidal (SHOW - **only approximate**)
- Irrespective of amount smoked as soon as you smoke, risk of CVD increases immensely



- Smoking also increases risk of airway problems
- E.g. smoker is 15-times more likely to develop COPD
- COPD def: - disease which slowly reduces your ability to breathe until you effectively suffocate
  - is irreversible: once it has started, cannot be stopped
- Only effective prevention and prevention is giving up smoking (slows progression to that of non-smoker)
- Risk of developing lung cancer is also increased by up to 25 times
- Contrast to CVD, disease-smoking the relationship linear (SHOW – **only approximate**)
- The more cancer-causing chemicals that get into your body the higher the risk
- Doesn't just depend on number of cigarettes smoked but also how hard you smoke
- From the CO reading we can see that you smoke relatively/quite/very hard
- Anything above 5 indicates current smoking and your reading was: .
- The leaflet you have received contains more information



## Appendix VII.III Debriefing letter (intervention)

Royal Free and University College Medical School  
Department of Epidemiology and Public Health  
University College London  
Gower Street Campus



HEALTH BEHAVIOUR UNIT  
2-16 Torrington Place  
London WC1E 6BT

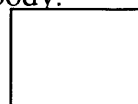
Telephone +44 (0)20 7679 6642  
Fax +44 (0)20 7813 2848  
Direct line +44 (0)20 7679 ....

Director *Professor Jane Wardle*  
Assistant Director *Professor Robert West*

### DEBRIEFING LETTER

Thank you for your participation in this study. The findings from this research will help us to understand how the chemicals in tobacco smoke differ between cigarette brands and how these chemicals are absorbed into the body.

CO reading:



As a reminder, all the information you provided during the survey will be kept strictly confidential. This project has been reviewed by, and received ethics clearance through the UCL Committee on the Ethics of Non-NHS Human Research (the contact there is: Ms Helen Dougal, Secretary of the UCL Committee on the Ethics of Non-NHS Human Research, Graduate School, North Cloisters, UCL, Gower Street, London, WC1E 6BT,

Should you have any questions or concerns about your participation in this study, please contact myself, Dr Ann McNeill or Helen Dougal.

If you would like any further information about the study, including a copy of our findings when they become available, please do not hesitate to contact us at the number below. Also, we would be happy to provide you with a list of smoking cessation resources, should you wish.

Thank you again for your help.

Sincerely,

Dr. Ann McNeill  
Dept. of Epidemiology & Public Health

University College London  
Phone: +44 (0)7968 585868  
email: [a.mcneill@ucl.co.uk](mailto:a.mcneill@ucl.co.uk)

Lion Shahab  
Dept. of Epidemiology & Public Health  
University College London  
Phone: +44 (0)20 7679 6645  
email: [lion.shahab@ucl.ac.uk](mailto:lion.shahab@ucl.ac.uk)

# Appendix VII.IV Ethical approval letter

Letter to Dr McNeill 26/05/2005

## Reporting Non-Serious Adverse Events.

For non-serious adverse events you will need to inform Ms Helen Dougal, Ethics Committee Administrator (h.dougal@ucl.ac.uk), within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair of the Ethics Committee will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

## Reporting Serious Adverse Events

The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

4. On completion of the research you must submit a brief report (a maximum of two sides of A4) of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

With best wishes

Chair of the UCL Committee for the Ethics of Non-NHS Human Research



**The Graduate School**  
University College London  
Gower Street London WC1E 6BT

**Professor Leslie C Aiello**  
Head of the Graduate School

Tel: 020 7675 7544  
Fax: 020 7675 7043  
Email: [gradschoolhead@ucl.ac.uk](mailto:gradschoolhead@ucl.ac.uk)

26 May 2005

**Dr Ann McNeill**  
Honorary Senior Research Fellow  
Cancer Research UK Health Behaviour Unit  
Department of Epidemiology and Public Health  
Brook House  
UCL  
2-16 Torrington Place

Dear Dr McNeill

**Re: Notification of Ethical Approval**

**Project ID: 0474/001: Cigarette testing protocols and human smoking behaviour study**

The above research has been given ethical approval following review by the Chair of the UCL Committee for the Ethics of non-NHS Human Research for a period of 12 months from the commencement of the project (1 June 2005) subject to the following conditions:

1. It is a requirement of the Committee that research projects which have received ethical approval are monitored annually. Therefore, you must complete and return our 'Annual Continuing Review Approval Form' PRIOR to the 1 June 2006. If your project has ceased or was never initiated, it is still important that you complete the form so that we can ensure that our records are updated accordingly.
2. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form'.
3. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. Both non-serious and serious adverse events must be reported.

The form identified can be accessed by logging on to the ethics website homepage: <http://www.grad.ucl.ac.uk/ethics/> and clicking on the button marked 'Key Responsibilities of the Researcher Following Approval'.

## Appendix VII.V Smoking and lung disease leaflet

**What Now?****Give up smoking before it is too late!**

Once you stop smoking your body can begin to repair the damage done by smoking. Most smoking-related diseases can be prevented if you quit smoking by middle age.

**Getting Help!**

**Stopping smoking is hard but it is possible. You are more likely to succeed if you get help.**

You can get help from your GP surgery or from a specialised smoking cessation service in your area. Call **0800 169 0 169** or text **GIVE UP** with your **full post code** to **88088** to find out about your nearest quit smoking service.

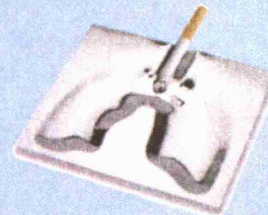
You can also get help from **free helplines**. These are staffed by trained, friendly counsellors. They will give you practical help & advice about stopping smoking & dealing with common problems such as weight gain.

**Freephone Helpline:** 0800 169 0 169  
[www.givingupsmoking.co.uk](http://www.givingupsmoking.co.uk)  
**Quitline freephone:** 0800 00 22 00  
[www.quit.org.uk](http://www.quit.org.uk)

**DON'T FORGET - QUITTING SMOKING IS THE SINGLE MOST HELPFUL THING YOU CAN DO TO FEEL BETTER & IMPROVE YOUR HEALTH**

**Smoking and your lungs**

Did you know that your GP can now prescribe effective treatment to help you stop smoking?



Going through the NHS Stop Smoking Services quadruples your chances of giving up successfully!

**Smoking, your lungs and your health - The Facts****BAD NEWS**

- 13 people die each hour because of smoking in the UK
- The average life-expectancy of smokers is reduced by **10 years**
- Smokers have a **1 in 2 risk** of getting ill & dying early from smoking - **9 out of 10** people with lung cancer are smokers
- Smokers are **15 times** as likely as non-smokers to develop emphysema, which makes breathing more difficult & results in physical inactivity, disability & death

**GOOD NEWS**

- ❖ New research shows that smokers who stop smoking have a **much lower risk** of acquiring emphysema - the earlier you quit the better
- ❖ Stopping smoking, even if you are well into middle age, will help you **avoid** developing **lung cancer**
- ❖ If you quit smoking you greatly **reduce your susceptibility** to lung infections & pneumonia
- ❖ Quitting smoking **improves breathing & slows progression** of emphysema
- ❖ If you stop smoking after developing a smoking related disease your chance of **survival improves**

**How does smoking affect your lungs?****When you smoke:**

- ▶ Debris gets into the lung, which turns it black
- ▶ The structure of the lung is damaged, which means that you take in less air with every breath
- ▶ The tissue of the lung is harmed, which leads to build-up of mucus that causes coughing & makes breathing harder
- ▶ The cells in the lung change, which causes lung cancer



## Appendix VII.VI Questionnaires T1, T2, T3

Questionnaire- T1	
v1.sex	<p>Circle: FEMALE / MALE</p> <p>If Female ask: Are you currently pregnant?</p> <p>➤ If No, continue</p>
v1.age	<p>How old are you? _____</p> <p>➤ If between 18 and 60, continue</p>
v1.cpd	<p><b>Note:</b> Insert answers from telephone questionnaire.</p> <p>Do you smoke every day? _____</p> <p>➤ If Yes, continue</p>
v1.cign	<p>How many cigarettes do you usually smoke <u>per day</u> ? _____</p> <p>➤ If 5 or more, continue</p>
v1.brncu	<p>What brand of cigarettes do you usually smoke?</p> <p>*Name, strength, size, flavour</p> <p><b>*Note: Research Assistant to confirm with pack</b></p>
v1.agest	<p>At what age did you start smoking daily?</p> <p>_____</p>
v1.cigsy	<p>How many cigarettes did you smoke yesterday?</p> <p>_____</p>
v1.wakin	<p>How long after waking do you usually smoke your first cigarette of the day?</p> <p>_____ Minutes</p> <p>_____ Hours</p>

v1.qt5yr	Have you quit smoking at all in the last five years? (Please circle)  YES / NO
v1.qtdat	<b>If yes:</b> When did your last quit attempt end?  _____ Months OR _____ Years
v1.qtlng	How long did you stop smoking?  _____ Days OR _____ Months OR _____ Years
v1.tobac	In the past 3 months, have you used any other tobacco products besides cigarettes, such as smokeless, cigars, pipe, bidis or kreteks, cigarettes other than study recognized, nicotine patch or gum or any other NRT products?"
v1.tobpr	Product: _____
v1.timeu	➤ <b>If yes, when was the last time you used it.</b>  _____
v1.ht	Finally, the last two questions will help us to understand the laboratory findings:  How tall are you?  _____ feet or _____ centimetres  _____ inches
v1.wt	How much do you weigh?  _____ pounds or _____ kilograms



Questionnaire T1/T2	
v2.int1	<p>Do you intend to stop smoking in the next month?</p> <p>1      2      3      4      5      6      7</p> <p>Definitely do not      Definitely do</p>
v2.susc1	<p>How likely do you think you are to develop any airway diseases?</p> <p>1      2      3      4      5      6      7</p> <p>Very unlikely      Very likely</p>
v2.self1	<p>How confident are you that you could stop smoking if you wanted to?</p> <p>1      2      3      4      5      6      7</p> <p>Very confident      Not confident at all</p>
v2.resp1	<p>Stopping smoking can reduce my risk of getting airway diseases.</p> <p>1      2      3      4      5      6      7</p> <p>Strongly disagree      Strongly agree</p>
v2.sev1	<p>Airway disease is a severe illness.</p> <p>1      2      3      4      5      6      7</p> <p>Strongly agree      Strongly disagree</p>
v2.wor1	<p>How worried are you about the impact of smoking on your health?</p> <p>1      2      3      4      5      6      7</p> <p>Very worried      Not worried at all</p>
v2.int2	<p>How likely is it that you will stop smoking in the next month?</p> <p>1      2      3      4      5      6      7</p> <p>Very unlikely      Very likely</p>
v2.susc2	<p>Compared with other people your age who are non-smokers, what do you feel is your risk of getting various airway diseases?</p> <p>1      2      3      4      5      6      7</p> <p>Much higher      A bit higher      About the same      A bit lower      Much lower</p>
v2.self2	<p>How easy would it be for you to stop smoking if you wanted to?</p> <p>1      2      3      4      5      6      7</p> <p>Not at all easy      Very easy</p>
v2.resp2	<p>I will be less likely to get airway diseases if I stop smoking.</p> <p>1      2      3      4      5      6      7</p> <p>Strongly disagree      Strongly agree</p>
v2.sev2	<p>Airway disease is a serious illness.</p> <p>1      2      3      4      5      6      7</p> <p>Strongly agree      Strongly disagree</p>
v2.wor2	<p>Are you afraid about the impact that smoking has on your health?</p> <p>1      2      3      4      5      6      7</p> <p>Not at all afraid      Very afraid</p>

**Questionnaire- T3**

Q 1	<p>Which of the following sentences describes you best (<b>Circle one</b>):</p> <p>(a) <u>Since being in the study</u> I have continued to smoke</p> <p>(b) <u>Since being in the study</u> I quit smoking but have started again For how long did you quit? _____</p> <p>(c) <u>Since being in the study</u> I have stopped smoking For how long? _____</p> <p>If you answered <b>a.)</b> please move on to <b>Question 4 (Q4)</b> If you answered <b>b.) or c.)</b> please move on to <b>Question 2 (Q2)</b></p>
Q 2	<p>Did you (<b>Circle one</b>):</p> <p>1) Plan to quit before giving up <b>or</b> 2.) Did you quit on spur of the moment?</p>
Q 3	<p>What made you give up? Was there a particular trigger? Please describe</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>If you <u>have started smoking again</u>, please move on to <b>Question 4 (Q4).</b> If you <u>have stopped smoking</u>, please move on to <b>Question 24 (Q 24)</b> on page 3</p>
Q 4	<p>On a scale from 1 to 7 (1 being very unlikely and 7 being very likely) how likely is it that you will stop smoking in the next month? (<b>Circle one</b>)</p> <p style="text-align: center;">1            2            3            4            5            6            7</p> <p style="text-align: center;">Very unlikely    Very likely</p>
Q 5	<p>How many cigarettes do you currently smoke a day? _____</p>
Q 6	<p>Which brand of cigarettes or tobacco do you smoke nowadays? _____</p>

	Over the <u>past couple of months</u> have you: <b>(Circle Yes or No)</b>
Q 11	(a) Talked to your family doctor about giving up smoking? Yes / No
Q 12	(b) Talked to nurse or other health professional about giving up smoking? Yes / No
Q 13	(c) Telephoned a stop smoking help line? Yes / No
Q 14	(d) Made appointment/went to Quit smoking service? Yes / No
Q 15	(e) Used nicotine replacement therapy (e.g. patches or gum)? Yes / No
Q 16	(f) Used a new non-nicotine therapy (eg. Zyban)? Yes / No
Q 17	(g) Tried another treatment to help you quit (e.g. acupuncture)? Yes / No
Q 18	If so, which treatment? _____
Q 19	(h) Set a date for when you will stop smoking? Yes / No
Q 20	(i) Cut down on cigarettes? ? Yes / No
Q 21	(j) None of the above? Yes / No
Q 22	(k) Anything else related to smoking? Please state: _____ _____ _____
Q 23	On a scale from 1 to 7 (1 being definitely do not and 7 definitely do), do you intend to stop smoking in the next month? <b>(Circle one)</b>  <div style="display: flex; justify-content: space-around; align-items: center;"> <span>1</span> <span>2</span> <span>3</span> <span>4</span> <span>5</span> <span>6</span> <span>7</span> </div> <div style="display: flex; justify-content: space-between; width: 100%;"> <span>Definitely do not</span> <span>Definitely do</span> </div>
Q 24	Is there anything else you would like to say about your participation in the study or about your smoking? _____ _____ _____ _____
Q 25	<p style="text-align: center;"><b>Many thanks for your help with this research. Unfortunately, we cannot provide you with individual data of the test results, but if you are interested in the study results, please provide us with an email address and we will send the results to you when they have been fully analysed.</b></p> <p style="text-align: center;">Interested? <input type="checkbox"/></p> <p style="text-align: center;">Email: _____</p>


















## Chapter IX

## Appendix IX.I Poster for Health Behaviour Research Centre Launch

## HYPERTENSION IN ENGLAND – ITS DIAGNOSIS IN RELATION TO SMOKING AND IMPACT ON SMOKING CESSATION

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Health Behaviour Research Centre 

## BACKGROUND

- Smoking and hypertension independently contribute to cardiovascular disease (CVD) and act synergistically to increase CVD risk<sup>1</sup>
- Clinical guidelines advise that efforts to detect and treat hypertension should be particularly high among people who smoke or display other CVD risk factors<sup>2,3</sup>
- However, little is currently known about the detection of hypertension among smokers and how this affects smoking behaviour
- This study therefore aimed to determine the level of diagnosis of hypertension in smokers and non-smokers, and to evaluate the impact of being diagnosed on motivation to stop smoking and smoking cessation

## METHOD

- 10506 adults participating in the 2003 Health Survey for England (HSE) - an annual cross-sectional household survey involving an individual home interview and nurse visit - were included in the analysis
- Demographic and smoking characteristics were assessed during the HSE interview and included age, sex, deprivation level, smoking status, nicotine dependence, motivation to quit and quit advice received
- Hypertension was considered diagnosed if participants indicated either that their doctor had told them they had hypertension or if they reported taking medication to control high blood pressure
- At the nurse visit, three blood pressure readings were taken 30 min after participants had last eaten, smoked, drunk alcohol or taken heavy exercise, and the mean of the last two readings used in analysis
- In line with guidelines<sup>3</sup>, actual hypertension was defined as receiving blood pressure treatment or as having a systolic blood pressure of  $\geq 140$  mm Hg and/or a diastolic blood pressure of  $\geq 90$  mm Hg

## RESULTS

- Objectively verified hypertension was present in 36.7% (95% CI 35.8-37.6) of the sample and more common among older, male, more deprived people and those in manual occupations; there were no differences in smoking characteristics (Table)

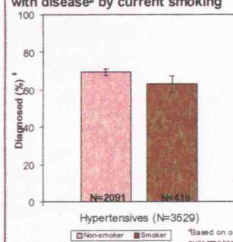
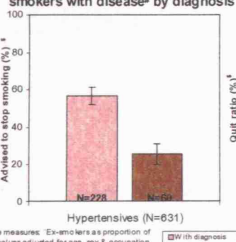
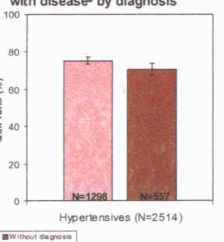
- Only two thirds of people with objective signs of hypertension in this sample were diagnosed (67.8%, 95%CI 66.4-69.3)

- After adjusting for confounders in logistic regression, smokers with hypertension were less likely to be diagnosed than non-smokers (OR 0.69, 95%CI 0.56-0.85; Figure 1)

Table: Demographic and smoking characteristics by hypertension status

	Total Sample (N=10506)	No hypertension (N=6649)	Hypertension <sup>a</sup> (N=3857)
<b>Demographics</b>			
Mean (SD) age	50.6 (18.1)	43.6 (16.3)	62.8 (14.2)***
% (N) male	44.6 (4684)	43.2 (2875)	46.9 (1809)***
% (N) manual occupation <sup>b</sup>	41.0 (4144)	38.3 (2441)	45.7 (1703)***
% (N) Lowest quintile IMD <sup>c</sup>	15.8 (1662)	14.9 (991)	18.5 (714)***
<b>Smoking characteristics</b>			
% (N) Current cigarette smoker <sup>d</sup>	20.0 (2098)	20.2 (1286)	19.8 (739)
% (N) Current smoker <sup>d</sup>	21.6 (2265)	21.8 (1389)	21.6 (803)
% (N) Ever Smoker <sup>d</sup>	63.7 (6689)	64.5 (4108)	63.6 (2369)
Mean (SD) cigarettes/day <sup>d,e</sup>	14.0 (8.0)	12.9 (9.8)	13.8 (8.5)
Mean (SD) dependence rating <sup>d,f</sup>	3.6 (1.0)	3.5 (1.2)	3.5 (1.0)
% (N) Motivated to quit <sup>g</sup>	69.5 (1325)	68.4 (893)	71.7 (387)

<sup>a</sup>Excludes pregnant participants; <sup>b</sup>Missing N=403; <sup>c</sup>Adjusted for age; <sup>d</sup>Adjusted for age, sex and occupation; <sup>e</sup>Cigarette smokers only; <sup>f</sup>Adjusted for age and occupation; <sup>g</sup>Smokers only; \*\*\*p<0.001

Figure 1: Diagnosis level among people with disease<sup>a</sup> by current smokingFigure 2: Quit advice among current smokers with disease<sup>a</sup> by diagnosisFigure 3: Quit ratio: among people with disease<sup>a</sup> by diagnosis

## DISCUSSION

- Hypertension was prevalent in this sample; smokers with signs of the disease were less likely to be diagnosed than non-smokers
- This finding is important when considering the consequences of receiving a diagnosis for the provision of quit advice and subsequent smoking cessation in hypertensives as demonstrated in this study
- Growing evidence showing a negative impact of smoking on acute blood pressure and progression of hypertension<sup>4</sup> underlines the on-going need to improve detection and treatment of hypertensive smokers

- While more smokers with a diagnosis were advised to stop smoking (OR 3.87, 95%CI 2.69-5.57; see Figure 2), they were not more motivated to do so (OR 1.24, 95%CI 0.85-1.82)

- People who had been diagnosed were more likely to have stopped smoking compared with hypertensives who had not been identified even after controlling for con- founders (OR 1.57, 95%CI 1.25-1.97; see Figure 3)

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